AN ANALYSIS OF THE CONTRIBUTION OF SMALL AIRWAYS TO LOWER AIRWAY RESISTANCE

By

JOHN NEWTON EVANS

A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA
1976

ACKNOWLEDGEMENTS

I wish to acknowledge and thank Dr. Marc J. Jaeger, Chairman of the Supervisory Committee, for his guidance and inspiration throughout my graduate study.

I would also like to express my thanks to the members of the Supervisory Committee, Dr. A. B. Otis, Dr. D. M. Travis, Dr. W. N. Stainsby and Dr. A. H. Nevis, for their suggestions and critical evaluation during my graduate training.

I would also like to recognize my fellow graduate students who provided constructive criticism and friendship through the years. I particularly wish to acknowledge the technical assistance and friendship of Ms. Linda Nichols and Ms. Patty Potter both of whom played a major role in the experiments reported herein.

I would also like to thank Dr. L. Wood for his guidance concerning techniques used in this study to measure resistance and Dr. S. Battista for his advice concerning placement of retrograde catheters in closed chest dogs. I also acknowledge Mr. J. Bolognese and

Dr. R. Marks for their statistical analysis of the data.

I would also wish to thank my parents who have provided encouragement and support throughout my education.

Most of all I wish to thank my wife, Ellen, and daughter, Melissa, for their love and understanding during my graduate training.

TABLE OF CONTENTS

Abstract of Dissertation Presented to the Graduate Council of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

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June, 1976

Chairman: Dr. Marc J. Jaeger
Major Department: Physiology

Total airway resistance is the frictional component of the pressure drop from the alveolus to the mouth related to the flow of gas at the airway opening. This resistance can be partitioned into an upper airway resistance, which includes the nose, larynx, pharynx and trachea and a lower airway resistance which includes the bronchi and small airways.

The lower airway resistance can be partitioned into contributions made by bronchi of various sizes. Peripheral or small airways can be defined as those which receive their blood supply from the bronchial circulation, as those upstream of the equal pressure point during forced expiration or as those peripheral to the size airway in which a pressure measuring device is located.

In this study pressure was measured with a retrograde

catheter wedged in bronchi which had a mean diameter of 3.0 mm. Therefore, peripheral resistance (R_P) refers to the resistance of airways less than 3.0 mm. in diameter; central resistance (R_C) refers to airways peripheral to the trachea and larger than 3.0 mm.; and lower airway resistance is the sum of R_P and R_C.

R_L and R_P were measured in the anesthetized and paralyzed dog at transpulmonary pressures (P_{tp}) of 15, 10 and 5 cm. H_2O, while the lungs were oscillated at 4 cycles per second. These measurements were made with the chest closed and following a sternal splitting procedure with wide retraction of the ribs. At a P_{tp} of 5 cm. H_2O in the closed chest dog the mean R_L and mean R_P in 13 dogs were 3.02 and 1.5 cm. $H_2O/L/S$, respectively. Following the opening of the chest R_L was unchanged at 2.99 cm. $H_2O/L/S$ while R_P was significantly ($p < .02$) reduced at .73 cm. $H_2O/L/S$. A similar effect of opening the chest was seen at P_{tp}'s of 15 and 10 cm. H_2O.

R_L and R_P were curvilinearly related to P_{tp} in both the closed and opened chest conditions. R_L was maximum at a P_{tp} of 5 cm. H_2O and was reduced at the higher pressures. R_P was lowest at a P_{tp} of 10 cm. H_2O.

Beta adrenergic receptor blockade with propranolol (1 mg./Kg. i.v.) did not change R_L or R_P in the dog when

the chest was intact. However, it did prevent the reduction of R_p upon opening the chest which had been observed in non-beta adrenergic receptor blocked animals.

Theoretical predictions of the contribution of airways less than 3.0 mm. in diameter are presented for both the human and dog lung using morphometric data and assuming laminar flow. The predictions agree with the in vivo measurements in the closed chest dog that up to 50% of the lower pulmonary resistance is contributed by airways less than 3.0 mm. in diameter.

It was shown that the contribution of peripheral airways to lower pulmonary resistance in closed chest dog is significantly greater than that measured following the opening of the chest. This reduction of peripheral resistance is mainly mediated through an increased beta adrenergic receptor stimulation in the peripheral airway. The influence of sympathetic input on the tonus of peripheral airway smooth muscle is minimal in the closed chest dog and only becomes significant when the chest is opened. In spite of the reductions in R_p due to opening of the chest there were no significant changes in R_L, which means that central resistance increased in a magnitude equal to the reduction of R_p. This suggests the possibility of the maintenance of a constant R_L at a given lung volume by coordinated changes in R_C to offset changes in R_p.

INTRODUCTION

This is a study of pulmonary resistance and in particular the contribution of airways less than 3 mm. in diameter to lower pulmonary resistance. For the first time the peripheral resistance was measured by means of a retrograde catheter with the chest closed and following a sternal splitting procedure in the same dog. In addition, measurements were made following the creation of a pneumothorax and after beta adrenergic receptor blockade in an attempt to explain differences in resistance between the closed chest and opened chest condition.

Respiratory physiologists and clinicians have been concerned with the resistance to air flow in the tracheobronchial tree for many years. Its measurement can be used in the diagnosis and in the evaluation of the treatment of lung desease. Resistance is the relationship of the driving pressure needed to overcome frictional forces opposing a given flow in or out of the respiratory system.

Rohrer (25) in 1915 was one of the first researchers to consider that the total resistance of the respiratory system could be partitioned into contributions made by various

segments of the airway. He applied fluid mechanical principles to morphometric data from the human lung and made predictions concerning the distribution of resistance in the lung. He estimated that 54% of the resistance was in the upper airways, that is, the nose, pharynx, larynx and trachea. The remaining 46% was in the bronchi and smaller airways. He also presented predictions concerning the distribution of the resistances in the lower airway, ascribing 70% to airways less than 1 mm. in diameter.

Small or peripheral airway function has become of great importance to respiratory physiologists and clinicians in recent years. It has been suggested (12) that these are the airways first altered in the pathogenesis of some types of obstructive lung disease and that if subtle changes were detectable at an early stage then the disease process could be reversed with appropriate treatment. Numerous tests have been suggested to study these areas of the lung; however, at this time there is no general agreement on the test of choice (11).

The term peripheral or small airway has been defined differently by various authors and it has become an arbitrary term and perhaps even confusing. A bronchus is both small and peripheral compared to the trachea, yet is both large and central compared to a respiratory bronchiole.

The range in diameter of the bronchi is quite large as can be seen in Table 1. The more peripheral an airway the smaller its diameter, the shorter its length and the larger the total cross-sectional area of its generation because of the large degree of branching. Previous investigators have used several criteria to classify the airways as small or large: 1) large airways are those which receive their blood supply from the bronchial circulation while small airways are those which receive their blood supply from the pulmonary circulation (21); 2) large airways are those which are larger than an airway which contains a pressure measuring device while small airways are smaller than the one which contains the catheter (13); 3) during forced expiration large airways are those downstream of the equal pressure point while small airways are those upstream of the equal pressure point (18). In this paper small will be synonomous with peripheral and large will be equivalent to central. Definition 2 will be used to functionally classify the airways. In general the catheter was placed in airways 2.8 to 3.2 mm. in diameter. Therefore airways less than 3.2 mm. in diameter are classified as peripheral.

The pressure can be measured at various points in the system and pairs of these pressures can be used to measure different pressure drops, which can be used to compute

Table 1. Nomenclature and dimensions for human bronchial tree based on data of Weibel (31).

Generation	Name	Diameter (cm)	Length (cm)	Total Cross Section (cm^2)
0	Trachea	1.8	12.0	2.54
1	Main Bronchi	1.22	4.76	2.33
2	Lobar Bronchi	0.83	1.90	2.13
3	Segmental Bronchi	0.56	0.76	2.00
4	Subsegmental Bronchi	0.45	1.27	2.48
5		0.35	1.07	3.11
thru	Small Bronchi			
10		0.13	0.46	13.4
11		0.109	0.39	19.6
thru	Bronchioles			
13		0.082	0.27	44.5
14		0.074	0.23	69.4
and	Terminal Bronchioles			
15		0.066	0.20	113.0
16		0.060	0.165	180.0
thru	Respiratory Bronchioles			
18		0.050	0.117	534.0
19		0.047	0.099	944.0
thru	Alveolar ducts			
23		0.041	0.050	11,800.0
24	Alveoli	244 μm	238 μm	43-80 m^2

resistances of different sections of the airway. The respiratory system is schematically shown in Figure 1 with examples of points indicated where pressure can be measured. Definitions of some of the symbols to be used in this paper are shown in Table 2.

Since the lung is located within the thorax it is necessary to estimate the surrounding pressure of the lung to eliminate the elastic pressure of the chest wall. This may be accomplished in part by opening the chest in the experimental animal, which makes the surrounding pressure equal to atmospheric pressure or by measuring the pleural pressure (P_{pl}) in the intact subject (20).

The pressure in the trachea (P_{tr}) can be measured by inserting a pressure sensing device between the cartilaginous rings into the trachea. The pressure at the airway opening (P_{ao}) can be determined by measuring the lateral pressure at that point. The measurement of bronchial pressure (P_{br}) poses a problem. If a catheter is passed into a small bronchus it may obstruct flow and result in erroneous values. In an early study Sonne (28) in an attempt to measure alveolar pressure pulled catheters through the parenchyma of the lung and wedged them in the periphery of the lung. Macklem and Mead (13) have refined this technique and have made lateral pressure measurements in bronchi (P_{br})

Figure 1. Schematic representation of the respiratory system including the chest wall, lung and airways. Shown are points where pressure can be measured and the pressure drops which can be determined using pairs of these pressures.

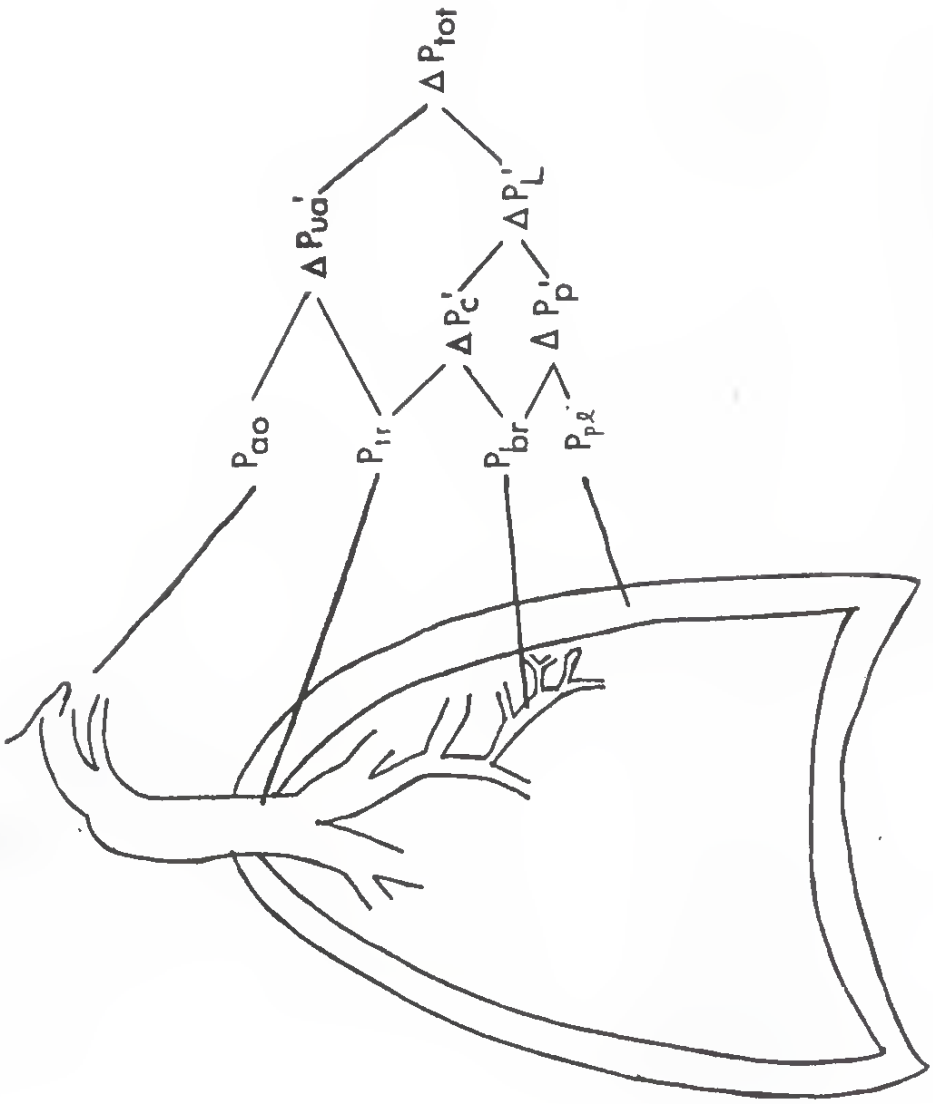

ΔP tot
ΔP ua'
ΔP L'
ΔP c'
ΔP p'
P ao
P tr
P br
P pl

Table 2. Definitions of symbols used in this paper.

Symbol	Definition
P_{pl}	pleural pressure
P_{br}	lateral pressure in the bronchus
P_{tr}	lateral pressure in the trachea
P_{ao}	lateral pressure at the airway opening
ΔP_P'	$P_{pl}-P_{br}$; peripheral pressure drop includes a resistive, elastic and inertial component
ΔP_C'	$P_{br}-P_{tr}$; central pressure drop includes a resistive and inertial component
ΔP_L'	$P_{tr}-P_{pl}$; lower pulmonary pressure drop includes an elastic, resistive and inertial component
ΔP_{ua}'	$P_{ao}-P_{tr}$; upper airway pressure drop includes a resistive and inertial component
ΔP_{TOT}'	$P_{ao}-P_{pl}$; total pressure drop includes a resistive, elastic and inertial component
ΔP_P	resistive pressure drop in the periphery of the lung
ΔP_C	resistive pressure drop in the central airways
ΔP_L	resistive pressure drop in the lower airways
R_P	resistance in the peripheral portions of the lung includes airway and tissue resistance
R_C	resistance in the central airways includes airway resistance
R_L	resistance in the lung includes airway and tissue resistance

by wedging the catheters in the wall of the airway. In this method the catheter does not impede flow between the carina and the point of measurement.

The difference between the bronchial pressure (P_{br}) and pleural pressure (P_{pl}) is called the peripheral pressure drop ($\Delta P'_p$). During the breathing cycle it consists of an elastic component (P_{el}) related to lung volume, a resistive component (P_R) related to friction of air flow through the airways ($P_{R_{fr}}$) and to the resistance of the tissue to deformation ($P_{R_{tiss}}$) and an inertial component (P_{IN}) related to the acceleration of gas.

$$\Delta P'_p = P_{el} + P_R + P_{IN}$$

$$P_R \rightarrow P_{R_{fr}},\ P_{R_{tiss}}$$

The difference between the bronchial pressure (P_{br}) and tracheal pressure (P_{tr}) is the central pressure drop ($\Delta P'_C$). It consists of a resistive component (P_R) related to the friction of air flow through airway ($P_{R_{fr}}$) and an inertial component (P_{IN}) related to the acceleration of gas.

$$\Delta P'_C = P_R + P_{IN}$$

$$P_R \rightarrow P_{R_{fr}}$$

The peripheral pressure drop ($\Delta P_P'$) and the central pressure drop ($\Delta P_C'$) can be added together to obtain the total pulmonary pressure drop ($\Delta P_L'$). This represents the total pressure drop from the pleural space to the trachea.

$$\Delta P_L' = \Delta P_P' + \Delta P_C'$$

$$\Delta P_L' = P_{el} + P_R + P_{IN}$$

$$P_R = P_{R_{fr}} + P_{R_{tiss}}$$

The difference between the tracheal pressure (P_{tr}) and the airway opening pressure (P_{ao}) is the upper airway pressure drop ($\Delta P_{UA}'$). It consists of resistive component (P_R) related to the flow of air (P_{fr}) and an inertial component (P_{IN}) related to the acceleration of gas.

$$\Delta P_{UA}' = P_R + P_{IN}$$

$$P_R = P_{R_{fr}}$$

The upper airway pressure drop ($\Delta P_{UA}'$) can be added to the lower airway pressure drop ($\Delta P_L'$) to obtain the total pressure drop ($\Delta P_{TOT}'$) from the pleural space to the airway opening.

$$\Delta P_{TOT}' = \Delta P_{UA}' + \Delta P_{P}' + \Delta P_{C}'$$

$$\Delta P_{TOT}' = P_{el} + P_{R} + P_{IN}$$

$$P_{r_{fr}} \quad P_{R_{tiss}}$$

To obtain the resistance in each of these sections it is necessary to relate the resistive component (P_R) of that section to the flow ($\dot{V}$) of gas through the system. Therefore, one can compute total resistance (R_{TOT}), peripheral resistance (R_P), central resistance (R_C), lower pulmonary resistance (R_L) or upper airway resistance (R_{UA}).

$$R_{TOT} = R_{UA} + R_{L}$$

$$R_{TOT} = R_{UA} + R_{P} + R_{C}$$

Predictions of Peripheral Resistance Based on Anatomic Data

As previously stated, Rohrer (25) predicted that 70% of lower airway resistance was in airways less than 1 mm. in

internal diameter. His predictions were based on anatomical data obtained from an excised human lung, which had collapsed to zero volume. According to Weibel (31), Rohrer underestimated the total number of airways less than 4 mm. in internal diameter and therefore overestimated the pressure drop peripheral to that size. Weibel's data are perhaps more relevant to the intact lung because it was obtained from human lungs which had been inflated to 75% of total lung capacity prior to fixation. These more recent measurements suggest that the peripheral resistance should be considerably less than predicted by Rohrer because of the underestimation of total cross-sectional area of the airways in the periphery.

All of the data obtained from anatomical studies of excised lungs are open to criticism when extrapolations are made to the intact lung. When the measurements on the excised lung are made the effects of nervous input and of circulating active compounds have been removed. The alteration in the tonus of the smooth muscle in a non-living preparation could alter the resting diameters and lengths observed compared to the intact animal. In addition, fixation of tissue may result in errors in size relative to the in vivo condition.

Green (7) has used the anatomical data of Weibel (31)

to estimate flow resistance of each generation of the human lung. Assuming laminar flow and a regular dichotomous branching pattern of the tracheobronchial tree he applied Poiseuille's law. He found that the maximal resistance occurs at the sixth generation and the resistance of each generation becomes less as one moves peripherally and the airways become smaller. The apparent discrepancy of the smaller tubes having a lower resistance is explained by the increase of total cross-sectional area of each generation and the reduction in length of the daughter compared to parent airways. According to the Poiseuille relationship the pressure drop is inversely related to the cross-sectional area squared and is directly related to the length. Therefore, an increase in area with a simultaneous reduction in length must result in a reduced resistance.

Horsefield and Cumming (8) reported measurements made on a cast from a human lung inflated to five liters. They reported the branching in the bronchial tree to be by asymmetrical dichotomy, while in the lobules the branching is more symmetrical. They found, as did Ross (26) in the dog, that the number of terminal bronchioles arising from a bronchus of any given diameter decreased with increasing distance from the carina. They found 28×10^3 terminal bronchioles which is less than one half the number reported

by Weibel (31). Using their own data, they predicted that the structures in which the resistance to laminar flow is highest are the airways between 1 and 4 mm. in diameter.

Pedley et al. (24) have used the anatomical data of Horsefield and Cumming (8) to predict the pressure drop along the tracheo-bronchial tree and did not make the assumption of Poiseuille flow. They have taken into account the non-parabolic velocity profiles, which occur in all but the smallest airways. They found that the resistance in the larger airways calculated in this way is greater than if the Poiseuille equation is used, while there is little effect on the calculated resistance of the smaller airways.

Previous Measurements of Peripheral Airway Resistance by Retrograde Catheters

The retrograde catheter technique (13) is used to measure lateral pressure in small bronchi. The catheter is wedged in the bronchus and passes out through the parenchyma of the lung. If pleural pressure and tracheal pressure are also measured then the peripheral ($\Delta P'_P$), central ($\Delta P'_C$) and lower pulmonary pressure drop ($\Delta P'_L$) can be determined. The frictional component of each of these pressure drops can be related to flow to obtain peripheral resistance (R_P), central resistance (R_C) and lower pulmonary resistance (R_L).

In 1967 Macklem and Mead (13) measured the resistance of central and peripheral airways by means of a retrograde catheter wedged in airways 1.5 to 2.5 mm. i.d. Using an oscillatory technique the measurements were made in opened chest, living dogs and in excised lungs from various species. In this technique the lungs are oscillated at resonant frequency with a loudspeaker driven by a sine wave generator. It is a means by which the resistive component can be separated from the total pressure and resistance calculated by relating the resistive pressure to flow. They found that peripheral resistance was too small to detect above 80% of the vital capacity, but increased at lower volumes to 15% of R_L at 10% of the vital capacity. The authors stated that there did not appear to be any systematic qualitative differences between the flow resistance measured in opened chest dogs and that for excised lungs.

In 1969 Macklem et al. (15) conducted a similar series of experiments to study the contribution of a wider range of airways to lower pulmonary resistance. They found that, at 60 - 80% vital capacity, airways less than 3 mm. in diameter contribute 30 - 50% of R_L, those between 3 and 8 mm. in diameter contribute 15% to R_L and those larger than 8 mm. in diameter contribute 45% to R_L. At 25 - 50% of vital

capacity airways less than 3 mm. in diameter contribute 14 - 24% of R_L, those between 3 and 8 mm. contribute 55% of R_L and those larger than 8 mm. contribute 25% of R_L. The fact that airways less than 3 mm. i.d. account for only approximately 20% R_L at low lung volumes and for 40% at high volumes does not necessarily imply that resistance of the small airways increases at high volumes. Although there was a tendency for the resistance of airways less than 2 mm. i.d. to be higher at high lung volumes the difference was not significant. There was a sevenfold decrease from 1.08 to 0.14 cm. H_2O/liter/second in the resistance of airways of 3 to 8 mm. i.d. when compared at low and high lung volumes. It was concluded that the 3 to 8 mm. i.d. airways are responsible for the change in R_L with lung volume.

At 50% of vital capacity vagotomy reduced R_L from approximately 2.3 to 0.9 cm. H_2O/liter/second, a reduction which was due mainly to a decrease in resistance of the 3 to 8 mm. i.d. airways. In all dogs studied the change in R_L with lung volume was reduced following vagotomy. The data indicate that the increase in R_L with decreasing lung volumes is mediated at least in part through the vagus and is a direct result of constriction of airways between 3 and 8 mm. i.d.

Woolcock et al. (35) found that upon cervical vagal stimulation the dogs showed an increase in R_L due to an increase in both R_C and R_P. The responsiveness of individual dogs was variable; in several dogs the central airways showed a greater change, while in others the peripheral change was greater. In any given dog the response to vagal stimulation was reproducible throughout the experiment. In addition, dogs which showed only small changes in peripheral resistance upon vagal stimulation had no significant change in the static elastic properties of the lung, but dogs which showed a response in the peripheral airways had an increase in elastic recoil so that at a $\Delta P_L'$ of 30 cm. H_2O the vital capacity was only 86% of the control value. This means that a large increase in peripheral airway tonus reduced the capacitance of these airways or impeded the filling of alveoli. In none of the dogs did the compliance become frequency dependent.

Woolcock et al. (36) in 1969 described experiments which were designed to investigate the role of the sympathetic nervous system in the control of airway caliber at various sites along the tracheobronchial tree. The interaction of beta adrenergic blockade (.25mg./Kg.) and vagal stimulation was studied in nine dogs. Treatment with propranolol resulted in a decrease in R_C and a 236% increase in R_P. The absolute changes in R_C and R_P were similar in magnitude;

therefore no net change in R_L was observed . The mean value for the ratio of R_P to R_L increased from 13% to 26% when treated with propranolol. Vagal stimulation without beta blockade increased R_C 350% and R_P 700%. In response to vagal stimulation following beta blockade R_C increased 600% and R_P 2,075%. Section of the Ansa Subclavia nerve produced results which were similar to those obtained with propranolol, which supports the supposition that the drug's bronchial effects are due to its beta blocking action.

Wood (34) has used the retrograde catheter technique to study the effect of physical properties of gases on lower pulmonary resistance. He found that in airways smaller than 4 mm. resistance was independent of gas density. This confirms that flow in these regions is laminar in character. The more central airways were dependent on density demonstrating a non-laminar flow condition in these regions. At 35% of vital capacity it was found that R_P accounted for 30% of the lower pulmonary resistance. It was also reported that the peripheral resistance varied little with lung volume while the central component varied significantly.

In 1973 Battista et al. (3 , 4) described a technique for chronically implanting retrograde catheters in the peripheral airways of dogs. In the preparation the chest was intact and the dogs were able to breathe spontaneously

during the measurement of resistance. In addition, the dogs were lightly anesthetized and could be used for repeated studies. A catheter with a 4 mm. flare was used; therefore peripheral airways would be those having a diameter of less than 4 mm. In five dogs at functional residual capacity, the mean R_C was 0.65 cm. H_2O/liter/second and mean R_P was 1.65 cm. H_2O/liter/second and the mean R_L was 2.3 cm. H_2O/liter/second. This means that in these dogs the R_P/R_L ratio was 70%, a value equivalent to that predicted by Rohrer (25) but three times that found by Macklem and Mead (13).

Recently Silvers et al. (27) partitioned airway resistance in normal and emphysematous isolated human lungs. During passive recoil at 50% of the vital capacity in four of six lungs R_P was more than 50% of R_L. The reduction in the tracheal length in this particular preparation has to be considered in evaluating the data. If lungs had been studied with the trachea intact, more resistance would have been added to the central component and a smaller R_P/R_L ratio would have been observed.

In summary there is a discrepancy in both the measured and predicted contribution of peripheral airways to lower pulmonary resistance reported by various investigators as seen in Table 3. Some of the discrepancy may be explained

by the difference in the size of the airway in which the catheter was wedged in the various preparations. However, there are other major differences between the conditions of the various preparations. For example, Battista et al. (3) measured resistance in the closed chest and spontaneously breathing dog, while Macklem and Mead (13) measured the resistance in the opened chest dog while the lungs were oscillated at resonant frequency.

The variation of peripheral resistance with lung volume appears also to be another disputed point. In Macklem and Mead's (13) results it decreases with increasing lung volume; the opposite is reported by Macklem et al.(15); while Wood (34) reports no lung volume dependence.

It is the purpose of this study to determine the contribution of peripheral airways in the closed and opened chest dog. In order to do this measurements were made at various transpulmonary pressures with the chest closed then at the same transpulmonary pressures following a procedure where the sternum was split and the chest widely spread. In addition, the effect of pneumothorax and beta receptor blockade on the contribution of peripheral airways was studied in an attempt to explain the difference between the closed and opened chest.

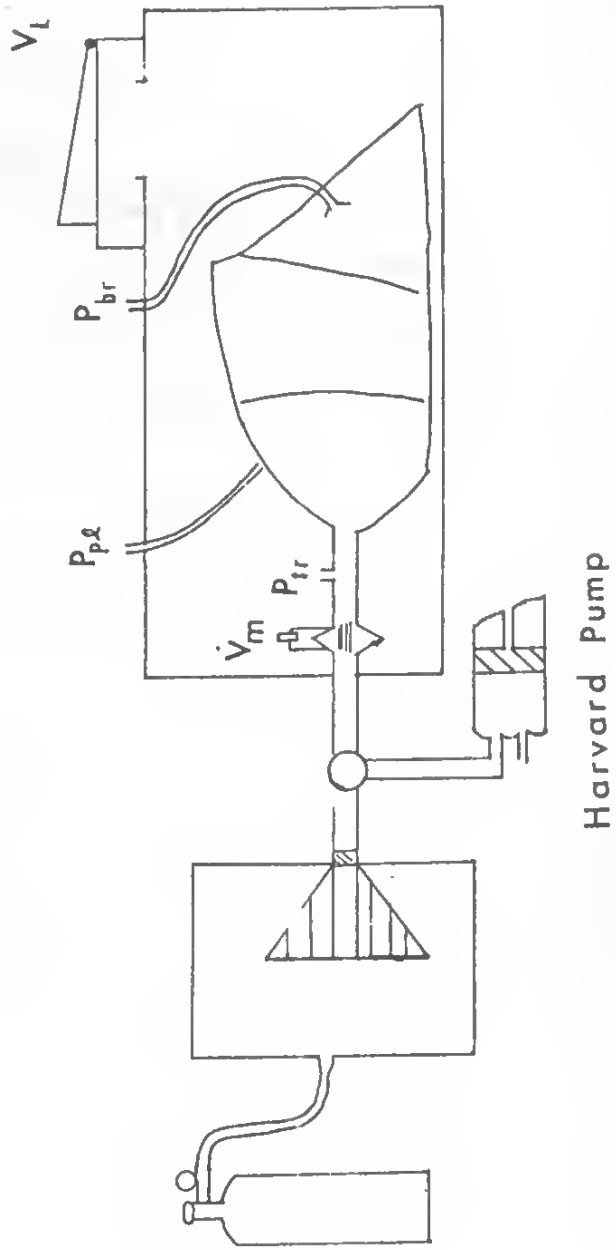
Table 3. Summary of data obtained by various investigators using the retrograde catheter technique.

Authors	Animal	Airway Size (mm.)	Lung Volume	R_P	R_L	R_P/R_L
				cm. H_2O/L/Sec.		
Macklem and Mead (13)	Dog	1.5 - 2.5	40% VC	0.17	1.70	0.10
Macklem et al. (15)	Dog	< 3.0	25-50% VC	0.35	1.90	0.18
Woolcock et al. (35)	Dog	.8 - 2.7	35% VC	0.21	1.20	0.18
Woolcock et al. (36)	Dog	< 3.0	35% VC	0.19	1.95	0.10
Battista et al. (4)	Dog	< 4.0	FRC	1.70	2.59	0.66
Silvers et al. (27)	Human	2.0 - 3.0	50% VC	0.85	1.51	0.56
Wood (34)	Dog	2.0 - 3.0	35% VC	0.48	1.56	0.31

METHODS

The experimental objectives required the development of techniques to measure lower pulmonary resistance (R_L) and peripheral reistance (R_p) in the dog with closed and opened chest at various lung volumes. This required the measurement of 1) lung volume; 2) flow rate of gas at the airway opening; 3) pleural pressure; 4) tracheal pressure; 5) bronchial pressure and 6) an estimate of alveolar pressure. A system diagrammed in Figure 2 was constructed and is described in detail in the following pages. The intact dog is placed within a plethysmograph and all measurements are made in the supine position. The oscillatory technique (5), which is described in more detail later in this section, was chosen for several reasons. It is a method that generates high flow rates with relatively small volume excursions and allows for the development of a relatively high frictional component in the pressure drop. It also provides a convenient method for applying positive pressure to the lung to place it at different volumes without interfering with the measurements. Since one of the objectives was to compare

Figure 2. Diagram of the equipment used in the experiments. For clarity, only the lungs are shown; however, in the actual experiments the intact dog was placed within the plethysmograph in the supine position.


V_L
P_{br}
P_{pl}
$\dot{V}_m$
P_{tr}
Harvard Pump

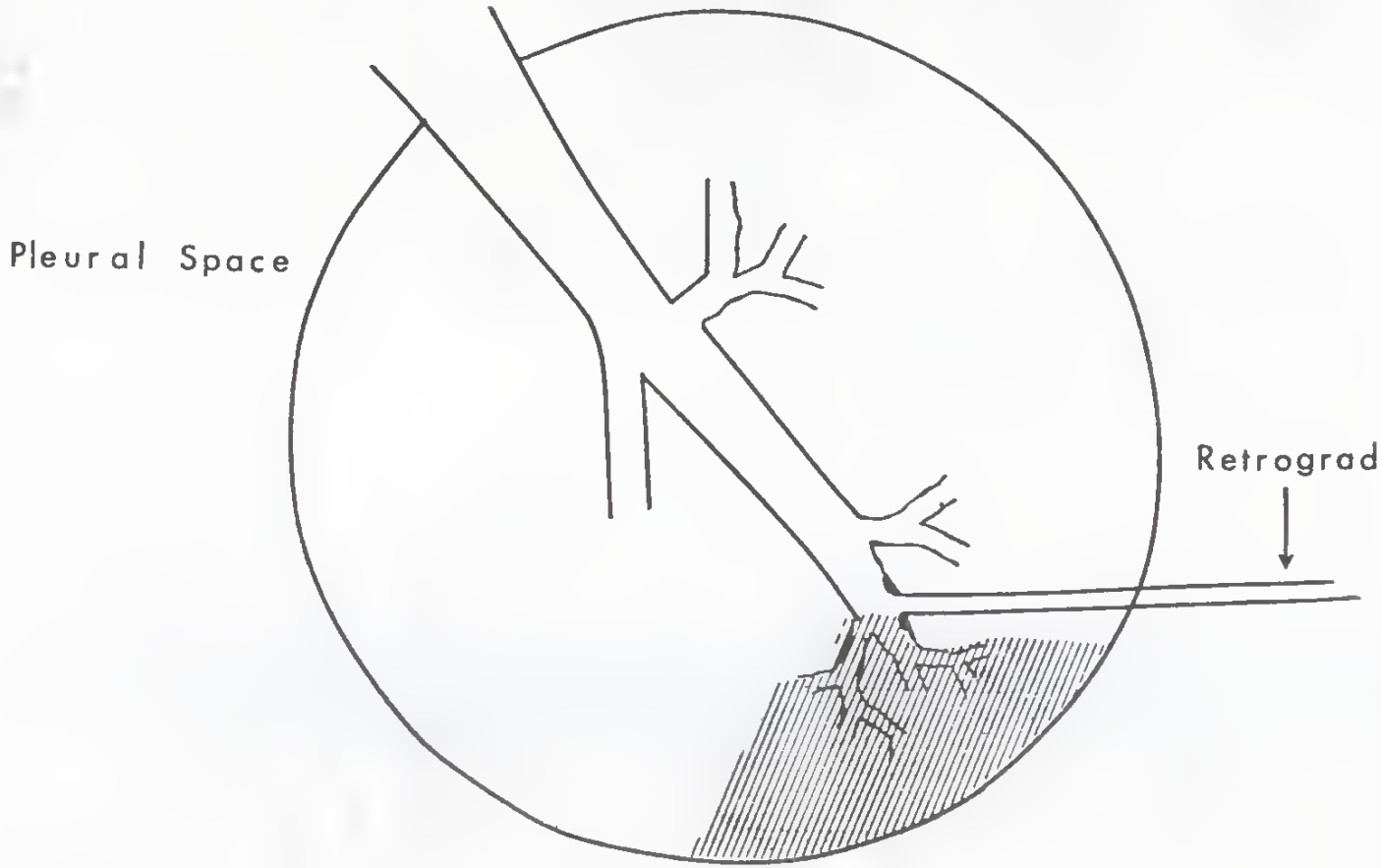
the opened chest results of this study to previous authors' (13) the use of similar techniques was judged appropriate.

Justification of the Retrograde Catheter Technique

Compared to methods in which the pressure measuring device is passed down the airway to the bronchus (14) the retrograde catheter technique offers the advantage of not obstructing the airway between the catheter tip and the airway opening. Undoubtedly, the catheter traumatizes the lung tissue through which it passes, and evidence of damage is often seen on autopsy. Air flow to areas peripheral to the catheter is altered; however, the affected region is quite small since the catheter is generally located less than 1 cm. from the surface of the lung. As can be seen in Figure 3 the areas which have been damaged by the catheter are not those which receive flow from the bronchus where the lateral pressure is measured. Rather it is an adjacent area, which is presumed to have suffered insignificant damage that is measured.

In their discussion of the technique, Macklem and Mead (13) have established limits on the effect the catheter could have on flow. One extreme is that the catheter would have no adverse effect and, therefore, the pressure measurements are accurate. The other extreme is that there is no flow

Figure 3. Diagram of a portion of the lung with the retrograde catheter wedged in a small bronchus. The shaded area is that portion of the lung which receives its ventilation from the bronchus where lateral pressure is measured.


Pleural Space
Retrograde Catheter

past the catheter. In this case the bronchus into which the catheter opens would act as an extension of the catheter and the pressure would be measured at the nearest branch point toward the hilus where flow is occurring. Since the pressure is measured at a more central point than the location of the catheter tip, the pressure drop between the alveolus and catheter may be overestimated. It seems reasonable to conclude that in cases between the extremes considered, one will overestimate the peripheral pressure drop.

Errors also result when lateral pressures are used to estimate pressure differences due to frictional resistance in a tube, if the linear velocities are different at the two points of measurement. In the airways this convective acceleration should lead to an overestimation of the pressure drop along the peripheral airways on deflation but to an underestimation on inflation, resulting in an asymmetrical inspiratory and expriatory pressure flow curve. Such asymmetry was not observed in the present experiments nor in those of Macklem and Mead (13). The acceleration pressure can be calculated according to Bernoulli's equation ($P_{ca} = \rho v^2/2g$), where ρ is gas density, v is linear velocity of the gas, and g is the acceleration due to gravity. Consider the trachea where the acceleration forces should be greatest because the linear velocities are the largest. If the diameter is 20 mm.

and the flow is 1 liter/second, then

$$\text{Flow} = 1000\ \text{cm}^3/\text{sec.}$$

$$\text{Diameter} = .2\ \text{cm.}$$

$$\text{Density} = 1.162 \cdot 10^{-6}\ \text{cm. } H_2O - \text{sec}^2/\text{cm}^2$$

$$v = \frac{\text{Flow}}{\text{Area}} = \frac{1000\ \text{cm}^3/\text{sec}^2}{\pi\ (.1\ \text{cm})^2}$$

$$v = 318.3\ \text{cm/sec}$$

$$P_{ca} = \frac{\rho v^2}{2}$$

$$P_{ca} = \frac{1.162 \times 10^{-6}\ \text{cm.}H_2O\text{-sec}^2/\text{cm}^2 \cdot (318.3\ \text{cm/sec})^2}{2}$$

$$P_{ca} = .0588\ \text{cm.}H_2O$$

In the present experiment a tracheostomy tube of 10 mm. i.d. was used, which could result in an overestimation of R_L due to convective acceleration of up to 0.96 cm.H_2O with expiratory flows of 1 liter/sec. Since the linear velocity of the peripheral airway is relatively small the effect of convective acceleration on the measurement of peripheral resistance should be minimal. An asymmetrical pressure flow curve was not observed for either the lower pulmonary

or peripheral pressures, indicating that the Bernoulli effect was minimal in the preparation.

If the traumatized area of the lung where the catheter is wedged has a mechanical influence on the adjacent area which is studied, then phase shifts between this part and the rest of the lung would be expected. Macklem and Mead (13) did not observe such phase differences in their study. They estimated dynamic compliance from the pressure difference between the catheter and the pleural surface and found it to be independent of frequency and the same as the dynamic compliance measured from transpulmonary pressure. If phase differences had been induced by the catheter then dynamic compliance measured using the retrograde catheter should have been frequency dependent and different from dynamic compliance measured by transpulmonary pressure. This type of analysis is dependent upon the assumption that a single bronchus is representative of all other bronchi in the lung of a similar size. In the normal lung, which is free of frequency dependence of compliance, this is probably true and is supported by the uniformity of results obtained by Macklem and Mead (13) and in the present study when the catheter is wedged in the same size airway of different lungs. The agreement between dynamic compliance determined from P_L and P_p also supports the assumption that the measurement is

representative of all airways that size.

Oscillation Technique

In the oscillatory technique (8) the lungs are connected to a loudspeaker, which is powered by a sine wave generator and driven at a frequency of about 4-5 cycles per second. The volume excursions are relatively small (40 ml.) and, therefore, the changes in pressure due to the elastic component are small, but because of the high frequency both the inertial and resistive components are relatively high.

Descriptions for electrical circuits in the study of alternating current have been developed and can be used by analogy in the analysis of the respiratory system when the breathing pattern is in the form of a sine wave. In this case the impedance can be calculated

$$z = \sqrt{R^2 + (\omega L - \frac{1}{\omega C})^2}$$

where z is the impedance, R is the resistance, ω is 2π times the frequency, C is the compliance and L the inertance. As frequency is increased from the normal breathing rate, to several cycles per second and $\omega L - \frac{1}{\omega C}$ approaches zero the impedance becomes dependent upon only the resistive

component of the pressure drop. This is the resonant frequency and if the pressure drop is measured it is equal to the resistive pressure drop, which if divided by flow will give the flow resistance of the system.

During quiet breathing, inertial pressure (P_{IN}) is negligible and $\Delta P_L'$ is the vector sum of P_{el} and P_R. Since the elastic pressure is in phase with lung volume, an increasing proportion of the volume can be subtracted from $\Delta P_L'$ until the corrected signal is in phase with flow (19). At that time the remaining pressure drop is due to resistance.

In the present experiments the lungs were oscillated at 4 cycles per second and pressure-flow relationships were observed on an oscilloscope. Loops were observed indicating that some part of the pressure drop was out of phase with flow. By electrically subtracting a proportion of volume (KV_L) from each pressure drop ($\Delta P_L'$ and $\Delta P_P'$) the loops were closed (19). Since the pressure drop was in phase with flow at this point, it is the resistive pressure drop and if divided by the flow, will give the flow resistance (R_P and R_L).

Volume (V_L), flow ($\dot{V}_M$), peripheral pressure drop (ΔP_P) and lower pulmonary pressure drop (ΔP_L) were recorded against time after loop closure. The peak to peak pressure

signals (ΔP_p and ΔP_L) were divided by the peak to peak flow signal ($\dot{V}_M$) to obtain resistance (R_P and R_L). Central resistance (R_C) was obtained by subtracting R_P from R_L.

Measurement of Flow, Volume and Pressure

Flow rate ($\dot{V}_M$) was measured with a Fleisch pneumotachograph and a Statham PM-97 differential pressure transducer. The pneumotachograph was mounted in the wall of the plethysmograph and could be connected to the tracheostomy tube to measure flow rate. The pneumotachograph and its pressure transducer gave a linear response to flows between $\pm$ 1.8 liters/second.

A whole body volume displacement plethysmograph, as seen in Figure 2, was constructed to accomodate medium sized dogs (12-18 Kg.). The change in lung volume was measured with a Krogh spirometer whose change in position was measured with Harvard apparatus rotary motion transducer. The plethysmograph had a total empty volume of 141 liters and was equipped with ports through which the catheters could be connected. The system was linear over the range used and had a flat frequency response up to 10 cycles per second.

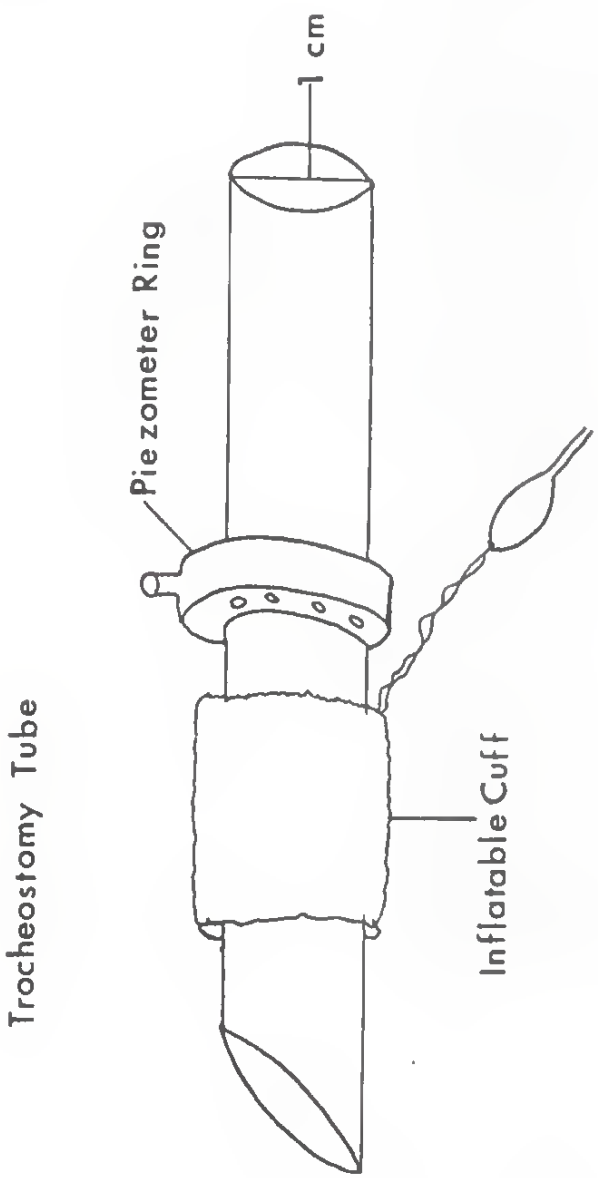
Two Statham PM 131tc differential pressure transducers were used to sense the airway pressures during the

experiments. One sensed the pressure difference between the pleural and tracheal pressures and the other between pleural and bronchial pressures. The two transducers were matched in sensitivity and were linear over the range of -50 to +50 cm. H_2O.

Pleural pressure was estimated using the esophageal balloon technique (37). The balloons were 5 cm. long and had a circumference of 3.14 cm. They were molded using liquid latex and made as thin as possible without leaking. They were mounted on polyethylene catheters 45 cm. long, which had an inside diameter of 1.67 mm. and an outside diameter of 2.41 mm. Prior to use, the volume range which results in a zero pressure for each balloon catheter was determined and a minimal volume in this range was used during the experiment. The balloon was passed down the esophagus and into the stomach so that positive deflections were observed on inspiration. It was then withdrawn until the pressure was negative relative to atmospheric pressure. The response of this system to a square wave change in pressure was better than 90% in less than 10 msec.

Tracheal pressure was measured using a piezometer ring, which was constructed as part of a tracheostomy tube as seen in Figure 4. The tube was 13 cm. long and had an inside diameter of 1 cm. The lateral pressure was measured 4.5 cm.

Figure 4. Tracheostomy tube with inflatable cuff and piezometer ring for measurement of lateral pressure. The cuffed end of the tube was placed within the trachea of the dog.


Trocheostomy Tube
Pie zometer Ring
1 cm
Inflatable Cuff

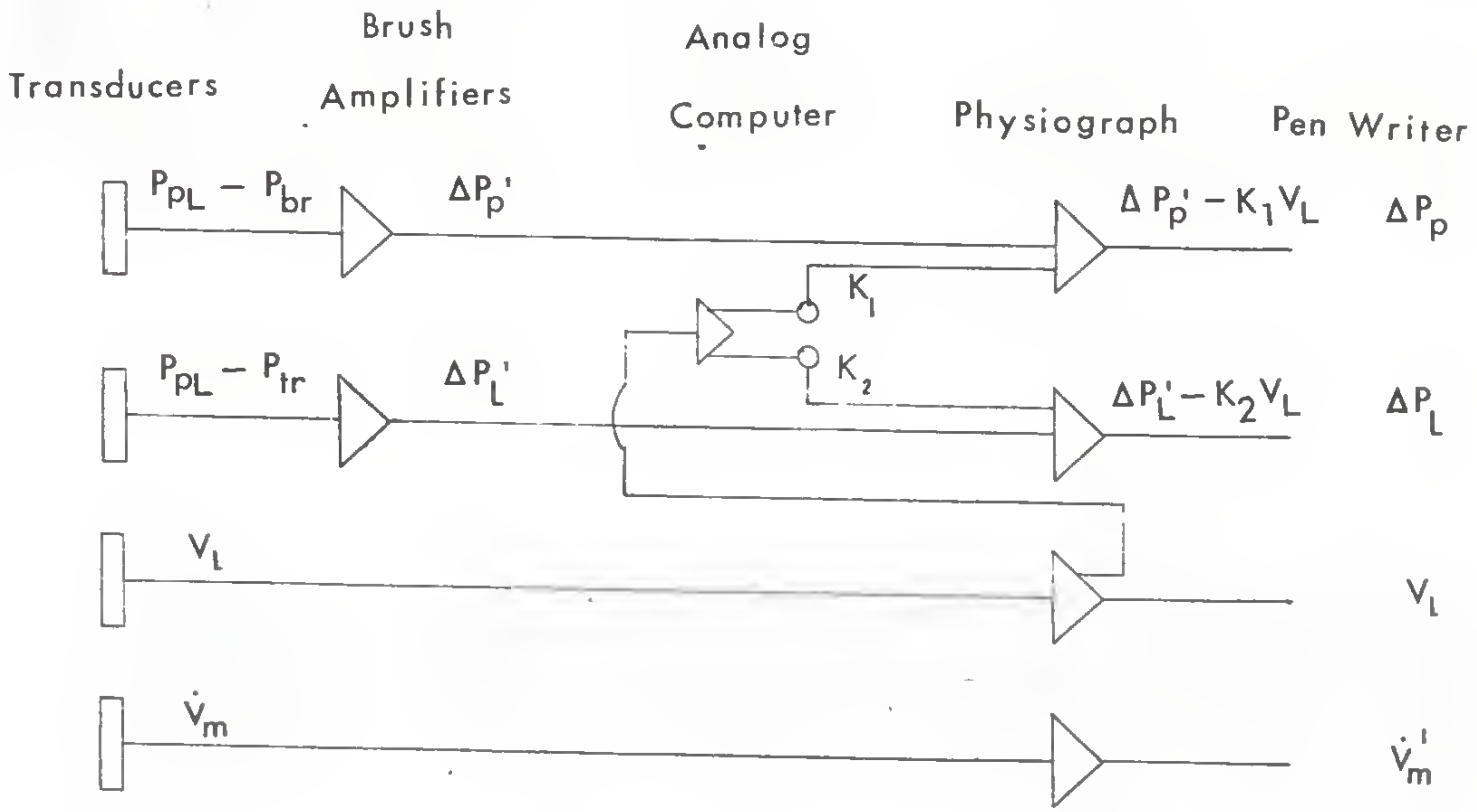
from the tip of the tube in the trachea. An inflatable cuff was slid over the tracheal tube, so that a leak proof seal could be made between the trachea and the tube itself.

The retrograde catheters were made from polyethylene tubing which had an inside diameter of 1.39 mm. and an outside diameter of 1.90 mm. One end was flared to a diameter of 3.0 mm. The overall length of the catheters was 75 cm. A thin suture was tied around the flared end of the catheter and was used in placement of the catheter and as a guide during the anatomical dissection at the termination of the experiment. The response of the catheter transducer system to a square wave change in pressure was better than 90% in less than 10 msec.

As seen in Figure 2, the dog lung could be connected to a Harvard ventilator or a loudspeaker by the appropriate positioning of a three way valve. An Acoustical Research model 5 loudspeaker was mounted in a sealed container and was powered by a sine wave generator. A positive pressure could be applied to the loudspeaker box and in turn to the airway opening. In this way various transpulmonary pressures could be attained while the lung was being oscillated at 4 cycles per second.

A schematic of the electronic system is shown in Figure 5.

Figure 5. Schematic of the electronics used in the experiment. The rectangles represent transducers, the triangles represent amplifiers and the circles potentiometers. After the subtraction of KV_L the pressure drops are the resistive pressure drops.


Transducers
Brush Amplifiers
Analog Computer
Physiograph
Pen Writer
$P_{pL} - P_{br}$
$\Delta P_p'$
$\Delta P_p' - K_1 V_L$
ΔP_p
K_1
K_2
$P_{pL} - P_{tr}$
$\Delta P_L'$
$\Delta P_L' - K_2 V_L$
ΔP_L
V_L
V_L
$\dot{V}_m$
$\dot{V}_m'$

The pressure transducers for airway pressure measurements were powered and amplified with two Brush transducer couplers and amplifiers. The transducer used in the determination of flow was powered by a Narco Biosystems straingauge coupler and amplified with a 7070 amplifier. The transducer used to sense the motion of the Krogh spirometer was powered by a Narco Biosystems transducer coupler and amplified with a 7070 amplifier. A Heathkit analog computer was used to subtract a proportion of the volume signal from the airway pressures as required in the oscillatory technique. All four signals ($\dot{V}$, V_L, ΔP_P and ΔP_L) were recorded on a Narco Biosystems Physiograph equipped with a rectilinear pen-writing system. The flow signal was also monitored as a function of the two airway pressures on a Tektronix model 5103N dual beam storage oscilloscope.

One cc. heparinized tuberculin syringes were used to obtain .5 cc arterial blood samples anaerobically from a catheter placed in the femoral artery. The samples were analyzed using a Radiometer Blood Micro System for pH, P_{CO_2} and P_{O_2} by standard techniques.

Mongrel dogs which were maintained by the Animal Resources Department were used in these experiments and all were treated in accordance with the American Physiological Society's Guidelines for Laboratory Animal Care.

The dogs were anesthetized with sodium pentobarbital (27 mg./Kg. i.v.), intubated and prepared for surgical procedures. Catheters were placed in the femoral artery and vein for blood gas analysis and drug infusion, respectively.

A tracheostomy was performed 2 cm. below the larynx and a cuffed tracheostomy tube inserted. A midline incision was made caudal to the sternum, the abdomen was opened and the diaphragm was exposed. The esophageal balloon was placed, as previously described, and the animal was allowed to stabilize.

Placement of the Retrograde Catheter

A polyethylene catheter, larger than the retrograde catheter was guided into the lower right lobe of the lung with a bronchoscope. The catheter was passed peripherally until resistance was encountered. A small amount of air flow was applied to the catheter, which presumably expanded the airways peripheral to the tip of the catheter and allowed its movement more peripherally. When the guide catheter was as peripheral as possible a piano wire was passed through it down to the peripheral airway, gently passed through the lung parenchyma and diaphragm and grasped through the abdominal incision. At this point one end of the wire was

visible at the trachea and the other in the abdomen. The guide catheter was removed and the wire was left in place. The retrograde catheter was then passed over the wire and guided peripherally along the path of the wire. The catheter was passed through the lung parenchyma and diaphragm and grasped in the abdomen. The guide wire was then removed. Finally the catheter was moved peripherally until the flared end became wedged in a peripheral bronchus.

The dog was then placed in the plethysmograph in the supine position and the catheters connected to the appropriate transducers. Following a period of spontaneous breathing the dog was paralyzed with succinylcholine (1.5 mg./Kg. i.v.) and ventilated with a Harvard constant volume ventilator. The paralyzed condition was maintained with supplemental infusions of succinylcholine. A quasi-static pressure-volume curve was obtained by inflating the lung to a pressure of 25 cm. H_2O and allowing it to deflate in 5 cm. H_2O steps down to functional residual capacity. During this procedure transpulmonary pressure and total pressure as well as the change in lung volume were recorded.

Following a brief pause the lungs were reinflated to 25 cm. H_2O and allowed to deflate to transpulmonary pressures of 15, 10, and 5 cm. H_2O while being oscillated at

4 cycles per second. By the method previously described, the pressure-flow loops monitored on the oscilloscope were closed and the corrected pressure drops (ΔP_P and ΔP_L) recorded as a function of time along with $\dot{V}_M$ and V_L. Using these measurements R_P, R_C and R_L were computed at each transpulmonary pressure.

Checks on the Patency of the Retrograde Catheter

Since there was frequent blockage of the retrograde catheter, it was imperative to have criteria to determine its patency. The first of these was the identity of quasi-static pressure volume curves determined using $\Delta P_L'$ and $\Delta P_P'$. Since the major component on a quasi-static maneuver of these two pressure drops is P_{el} they should have equal amplitude unless the retrograde catheter was blocked. A similar consideration applies to the total amplitude of $\Delta P_L'$ and $\Delta P_P'$ monitored at normal breathing frequencies. Equality in their amplitudes under these conditions was also considered as evidence for patency of the catheter. During oscillations a blockage of the catheter resulted in a reversal of the pressure-flow loop and a reduction in the amplitude of ΔP_P. The presence of any of these three conditions could usually be alleviated by flushing the retrograde catheter with air and the experiment continued.

At the completion of all experiments the dogs were sacrificed by an intravenous injection of KCl. The lungs were removed with the catheter intact and dried for three days at a transpulmonary pressure of 20 cm. H_2O. Each lung was then dissected, following the suture tied to the catheter, to determine the size airway in which the catheter was wedged.

The protocol described above was common to three series of experiments which had differences in their individual design.

Series I

Nine dogs were prepared as described above and the quasi-static pressure volume curve determined with the chest intact. Measurements of resistance (R_L and R_P) were made during oscillation at transpulmonary pressures of 15, 10 and 5 cm. H_2O. The sternum was then split and the chest widely spread with retractors. The dog was ventilated and expired against 5 cm. H_2O positive end-expiratory pressure (PEEP) to prevent collapse of the lung. Anesthesia and muscle paralysis were maintained at a level comparable to the closed chest condition. The quasi-static pressure volume curve was repeated and resistance determined during oscillation at transpulmonary pressures of 15, 10 and 5 cm. H_2O.

Series II

Six dogs which were included in Series I had pneumothoraces created between the closed and opened chest condition. After the closed chest measurements were made large bore tubes were placed between the 5^{th} and 6^{th} ribs and the quasi-static pressure volume curve determined. During oscillation the resistances (R_P and R_L) were determined at transpulmonary pressures of 15, 10 and 5 cm. H_2O. After obtaining the data in the pneumothorax condition the chest was opened and measurements were made as described in Series I.

Series III

Six dogs were prepared as described in the common protocol and the quasi-static pressure volume curve determined. R_L and R_P were measured during oscillation at transpulmonary pressures of 15, 10 and 5 cm. H_2O. Following beta adrenergic receptor blockade with propranolol (1 mg./Kg. i.v.)(23) the resistance measurements were repeated at transpulmonary pressures of 15, 10 and 5 cm. H_2O during oscillation with the chest intact. The sternum was then split and the chest wall widely retracted with maintenance of the beta adrenergic receptor blockade. The quasi-static pressure volume curve was determined. R_L and R_P were measured during oscillation at transpulmonary pressures of 15, 10 and 5 cm. H_2O. Throughout the

experiment a surgical level of anesthesia and muscle paralysis were maintained. As in the previous 2 series, ventilation was performed against 5 cm. H_2O PEEP once the chest was opened.

RESULTS

Series I

Figure 6 is a plot of the lower pulmonary resistance (R_L) and the peripheral resistance as a function of transpulmonary pressure (P_{tp}) for series I. Each point represents the mean of 13 dogs. R_L in both the closed and opened chest condition is curvilinearly related to P_{tp} with the greatest resistance observed at the lowest pressure. R_L's in the closed chest and opened chest conditions are not significantly different from each other when compared by multiple linear regression analysis (29). R_p in both conditions is also curvilinearly related to P_{tp} with a minimal value observed at a P_{tp} of 10 cm. H_2O. R_p is significantly ($p < .02$) reduced in the opened chest condition when compared to the values with the chest intact. At a P_{tp} of 10 cm. H_2O, R_p is reduced from 0.99 to 0.54 cm. H_2O/liter/second by opening the chest. This is a reduction to 54% of the control value. At this same pressure the R_p to R_L ratio is reduced from 50% in the closed chest to 33% in the open chest condition.

Figure 6. Mean peripheral resistance (solid lines) and lower pulmonary resistance (dashed lines) are plotted as a function of transpulmonary pressure for the 13 dogs of series I. Values for the closed chest condition are indicated by closed circles (●) and those for the opened chest condition are indicated by open circles (○). Transpulmonary pressures of 15, 10 and 5 cm H_2O in both the closed and open chest condition correspond to 97, 75 and 45% of the opened chest vital capacity. The lines between the points were drawn by eye.

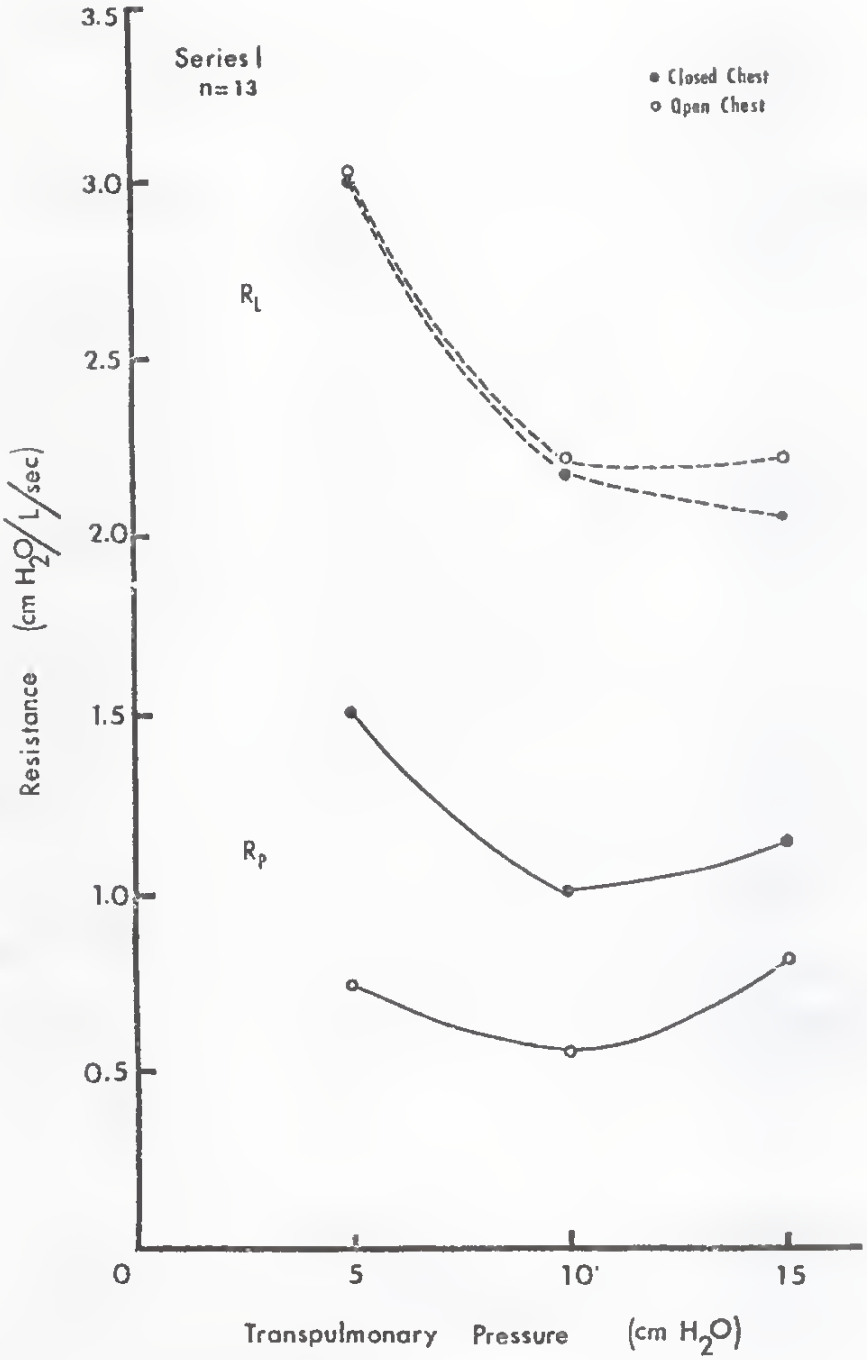

Series I
n=13
• Closed Chest
o Open Chest
R_L
R_P
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
5
10
15
Resistance (cm H_2O/L/sec)
Transpulmonary Pressure (cm H_2O)

Figure 7. The mean difference between the closed chest and opened chest for peripheral resistance (R_p) and lower pulmonary resistance (R_L) is plotted as a function of transpulmonary pressure. A positive difference means the opened chest resistance was less than the closed chest value. One standard error of the mean is shown above and below the mean.

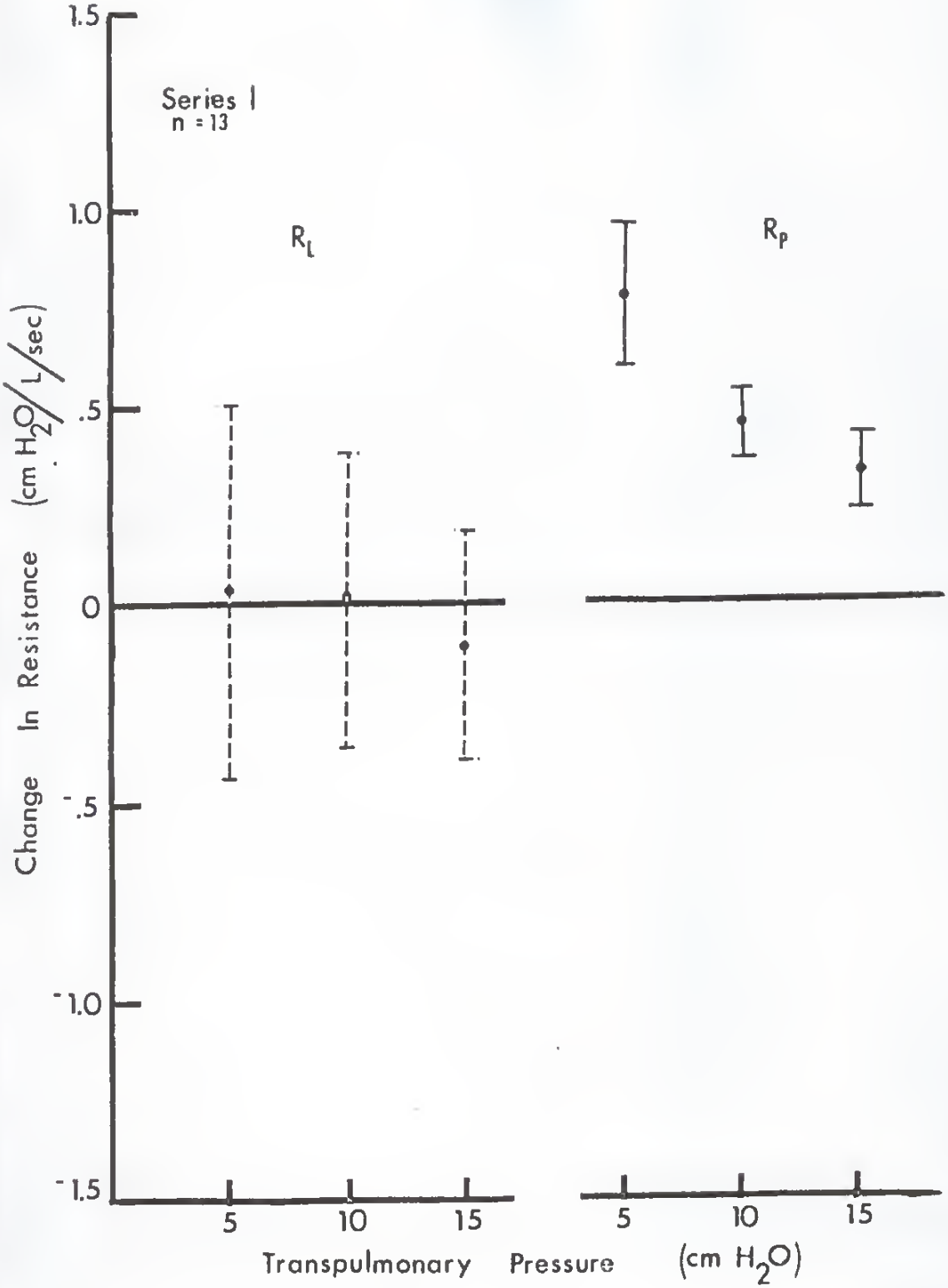

Series I
n = 13
R_L
R_P
1.5
1.0
.5
0
-.5
-1.0
-1.5
Change In Resistance (cm H_2O/L/sec)
5
10
15
5
10
15
Transpulmonary Pressure (cm H_2O)

Table 4. Individual data for the 13 dogs of series I. All values are expressed in cm.H_2O/liter/second. C = closed chest and O = opened chest.

P_{tp}	5 cm H_2O				10 cm H_2O				15 cm H_2O			
	R_L		R_P		R_L		R_P		R_L		R_P	
Dog	C	O	C	O	C	O	C	O	C	O	C	O
1	4.76	2.28	3.43	1.25	2.68	1.27	1.48	1.51	2.63	1.66	1.43	1.04
2	2.22	2.13	0.70	0.25	1.76	1.93	0.90	0.44	1.61	2.35	1.14	0.78
3	5.49	9.08	2.05	0.28	4.39	7.28	1.31	0.56	4.38	5.90	1.45	0.57
4	3.85	2.15	1.19	0.95	3.41	1.58	0.82	0.70	3.25	1.64	0.88	0.68
5	1.98	1.64	0.57	0.83	1.50	1.24	0.47	0.56	1.12	1.32	0.36	0.74
6	1.35	1.53	0.95	0.29	1.27	0.64	0.97	0.38	1.28	0.70	1.06	0.41
7	3.19	5.33	2.06	1.17	1.83	4.62	1.23	0.85	1.95	4.32	1.39	1.43
8	3.67	1.59	1.31	0.51	1.54	1.23	0.61	0.31	1.25	1.55	0.65	0.76
9	2.90	4.30	1.38	0.82	2.20	1.99	1.09	0.60	2.10	1.83	1.41	0.95
10	1.44	1.51	0.83	0.24	0.87	0.97	0.47	0.24	1.15	1.27	0.68	0.31
11	3.08	3.20	0.78	0.65	2.71	2.85	0.67	0.58	2.32	2.91	0.97	0.91
12	1.86	1.69	1.35	0.88	1.66	1.25	1.30	0.48	1.94	1.47	1.49	0.82
13	3.52	2.51	2.97	1.44	2.15	1.57	1.57	0.88	2.14	1.64	1.65	1.01
$\bar{x}$	3.02	2.99	1.50	0.73	2.15	2.18	0.99	0.54	2.04	2.20	1.12	0.80
s.e.	0.35	0.60	0.24	0.11	0.26	0.50	0.10	0.04	0.26	0.39	0.10	0.07

In Figure 7 the difference in resistance between the closed and opened chest conditions is plotted as a function of P_{tp} for R_L and R_P. Each point is the mean difference for the 13 dogs of series I on a paired basis and one standard error of the mean is drawn as a line above and below the point. Since the value for the open chest condition was subtracted from the closed chest condition value, a positive result indicates a reduction upon opening of the chest. The values for R_L were not significantly different from zero and indicate no change in R_L at any P_{tp} when the chest is opened. The differences for R_P were significantly ($p < .05$) different from zero, which means that R_P is reduced by opening the chest at all three P_{tp}'s tested. The differences appear to be dependent upon P_{tp} with the largest difference observed at 5 cm. H_2O.

Table 2 contains all individual data for the 13 dogs of series I. Included are the mean and standard error of the mean for each condition and each P_{tp}.

Series II

The results of series II, which demonstrate the effect of a pneumothorax, were plotted in the same format as series I. Figure 8 demonstrates the same curvilinear change of R_L and R_P with P_{tp} as was observed in series I. It may

Figure 8. Mean peripheral resistance (solid lines) and lower pulmonary resistance (dashed lines) are plotted as function of transpulmonary pressure for the 6 dogs of series II. Values for the closed chest are incicated by closed circles (●), values for the opened chest are indicated by open circles (o) and values in the presence of a pneumothorax are indicated by (X). Transpulmonary pressures of 15, 10 and 5 cm H_2O correspond to 97, 75 and 45% of the opened chest vital capacity. The lines between the points were drawn by eye.

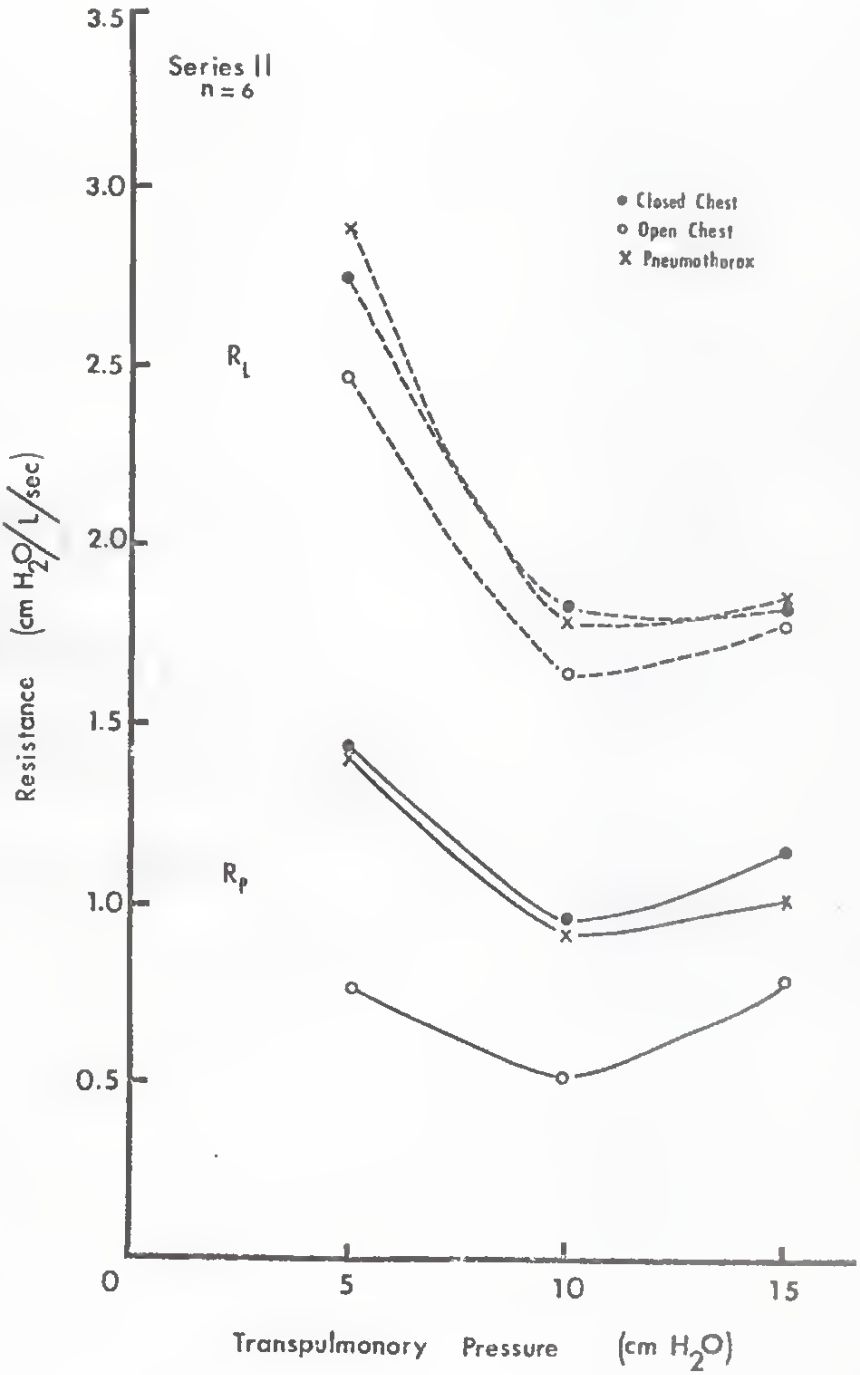

Series II
n = 6
• Closed Chest
o Open Chest
X Pneumothorax
R_L
R_P
Resistance (cm H_2O/L/sec)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
5
10
15
Transpulmonory Pressure (cm H_2O)

Figure 9. The mean difference between the closed chest and in the presence of a pneumothorax for peripheral resistance (R_p) and lower pulmonary reistance (R_L) is plotted as a function of transpulmonary pressure. A positive difference means the resistance in the presence of a pneumothorax was greater than with the chest closed. One standard error of the mean is shown above and below the mean.

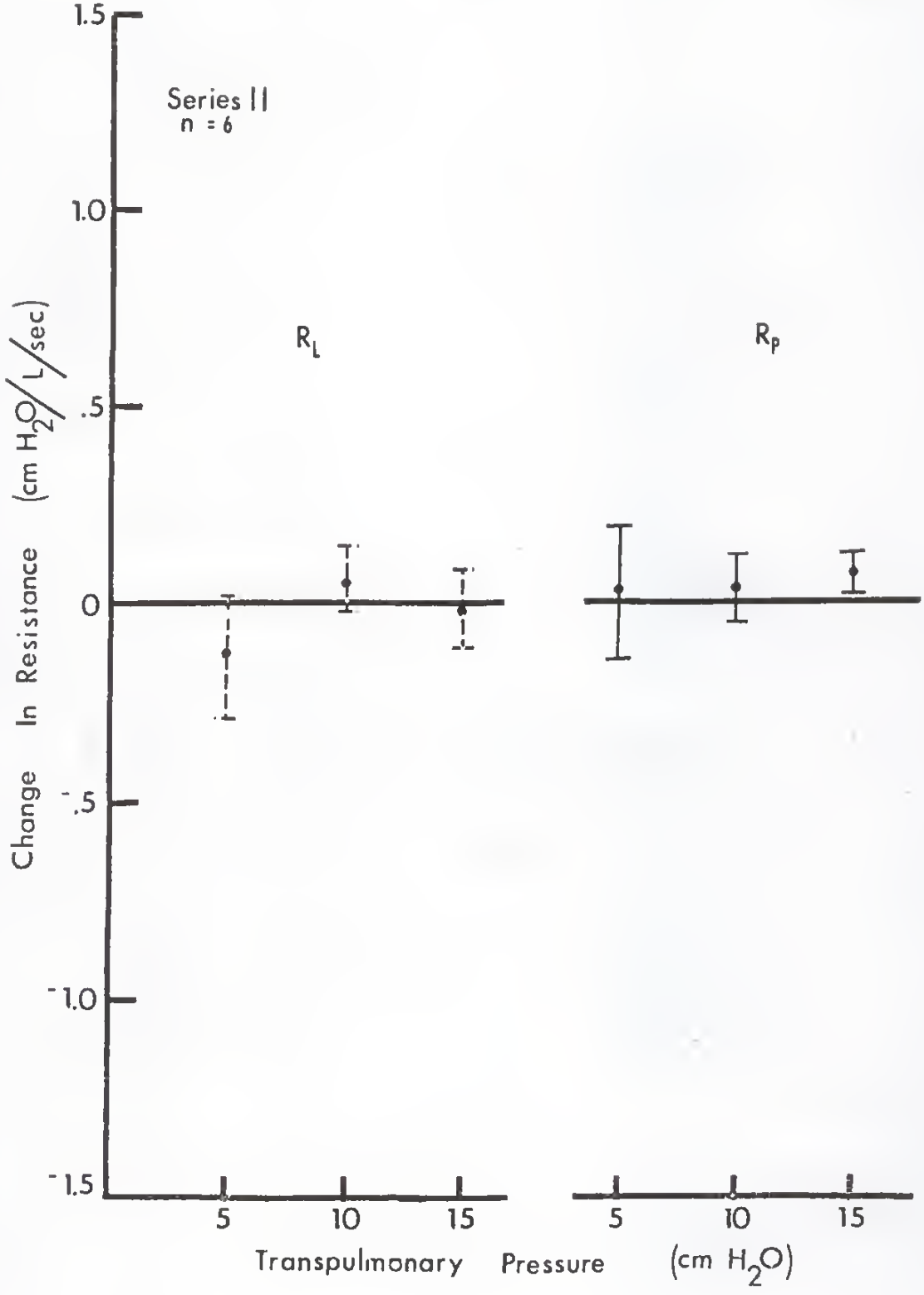

Series II
n = 6
R_L
R_P
1.5
1.0
.5
0
-.5
-1.0
-1.5
Change In Resistance (cm H_2O/ L/sec)
5
10
15
5
10
15
Transpulmonary Pressure (cm H_2O)

Table 5. Individual data for 6 dogs of series II. All values are expressed in cm.H_2O/liter/second. C = closed chest, P = pneumothorax and O = opened chest.

P_{tp}	5 cm H_2O						10 cm H_2O						15 cm H_2O					
	R_L			R_P			R_L			R_P			R_L			R_P		
Dog	C	P	O	C	P	O	C	P	O	C	P	O	C	P	O	C	P	O
8	3.67	3.50	1.59	1.31	0.78	0.51	1.54	1.68	1.23	0.61	0.48	0.31	1.25	1.76	1.55	0.65	0.48	0.76
9	2.90	3.49	4.30	1.38	1.30	0.82	2.20	1.95	1.90	1.09	0.91	0.60	2.10	2.00	1.83	1.41	1.20	0.95
10	1.44	1.51	1.51	0.83	0.66	0.24	0.87	1.06	0.97	0.47	0.56	0.24	1.15	1.04	1.27	0.68	0.57	0.31
11	3.08	2.74	3.20	0.78	1.48	0.65	2.71	2.37	2.85	0.67	0.99	0.58	2.32	2.25	2.91	0.97	0.73	0.91
12	1.86	1.91	1.69	1.35	1.38	0.88	1.66	1.59	1.25	1.30	1.12	0.48	1.94	1.73	1.47	1.49	1.31	0.82
13	3.52	4.08	2.51	2.97	2.82	1.44	2.15	2.11	1.57	1.57	1.44	0.88	2.14	2.24	1.64	1.65	1.78	1.01
$\bar{x}$	2.74	2.87	2.46	1.44	1.40	0.76	1.82	1.79	1.63	0.95	0.91	0.51	1.82	1.84	1.78	1.14	1.01	0.79
s.e.	0.36	0.40	0.45	0.32	0.31	0.16	0.25	0.18	0.27	0.17	0.14	0.08	0.20	0.17	0.23	0.17	0.20	0.10

be seen in both Figures 8 and 9 that the production of a pneumothorax does not change R_L or R_p significantly. However, the opening of the chest does result in a significant ($p < .02$) reduction of R_p. At a P_{tp} of 10 cm. H_2O the R_p's in the closed chest, in the presence of a pneumothorax, and opened chest conditions were 0.95, 0.91 and 0.51 cm. H_2O/liter/second, respectively. This represents an R_p to R_L ratio in the three conditions of 53, 51 and 32%, respectively.

Series III

Figure 10 is a plot of the mean lower pulmonary resistance (R_L) and mean peripheral resistance (R_p) as a function of transpulmonary pressure (P_{tp}) for the 6 dogs of series III. In all three conditions R_L varies curvilinearly with P_{tp} with a maximal value at the lowest P_{tp}. R_L in the closed chest; closed chest with beta adrenergic blockade or open chest with beta adrenergic blockade conditions are not significantly different from each other. R_p also varied curvilinearly with lung volume with the maximal value observed at the lowest P_{tp}. There was no significant difference between R_p closed chest, closed chest with beta adrenergic blockade or opened chest with beta adrenergic blockade.

Figure 10. Mean peripheral resistance (solid lines) and lower pulmonary resistance (dashed lines) are plotted as a function of transpulmonary pressure for the 6 dogs of series III. Values with the chest closed are indicated by closed circles (●), values with the chest closed with beta adrenergic blockade are indicated by (X) and values with the chest opened with beta adrenergic blockade are indicated by open circles (○). The lines between the points were drawn by eye.

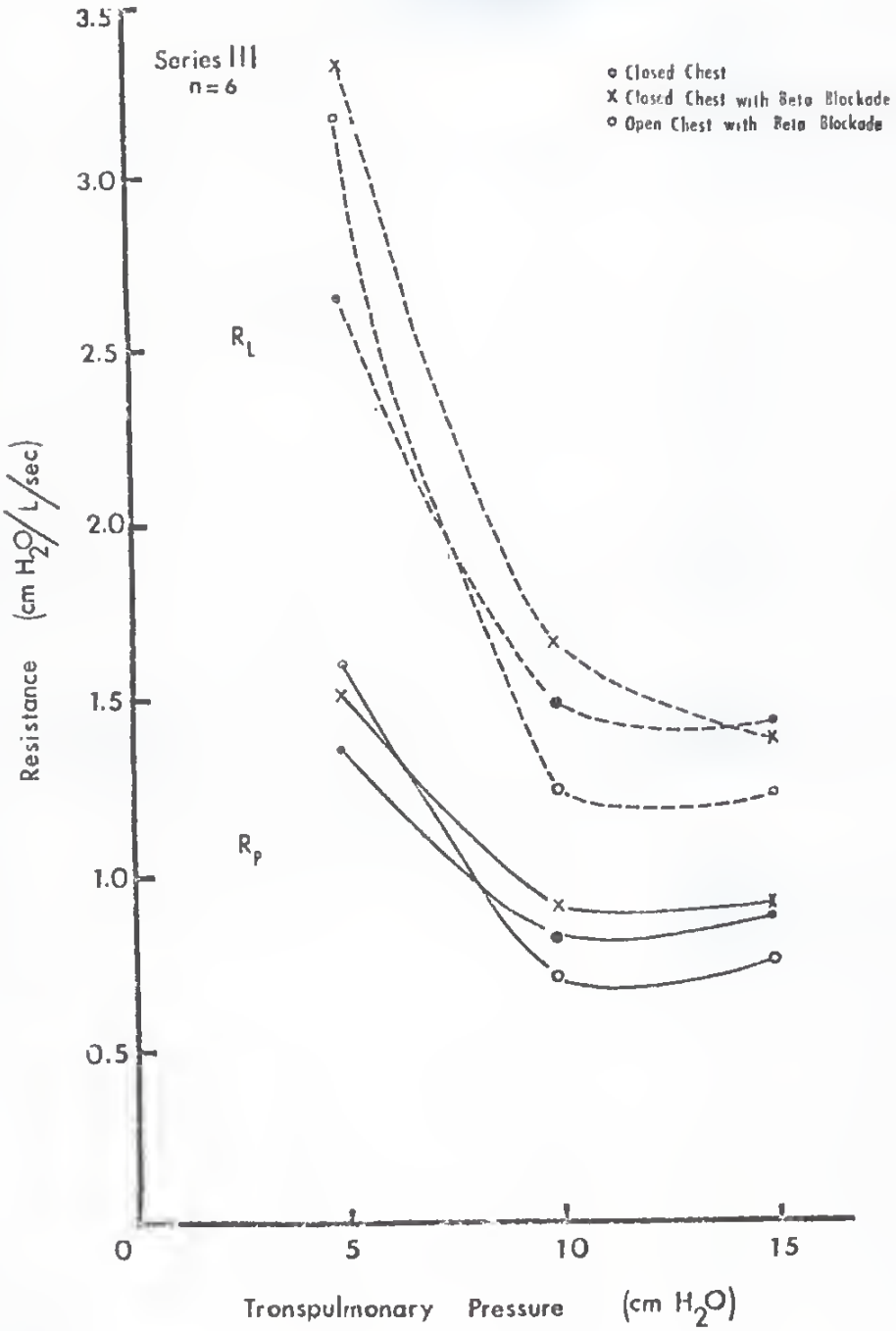

Series III
n = 6
o Closed Chest
X Closed Chest with Beta Blockade
o Open Chest with Beta Blockade
R_L
R_P
Resistance (cm H_2O/L/sec)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
5
10
15
Transpulmonary Pressure (cm H_2O)

Figure 11. The mean differences between the closed chest without beta adrenergic block and the opened chest with beta adrenergic blockade are plotted as a function of transpulmonary pressure. A positive difference means the resistance with the chest opened with a beta adrenergic blockade is less than with the chest closed. One standard error of the mean is shown above and below the mean.

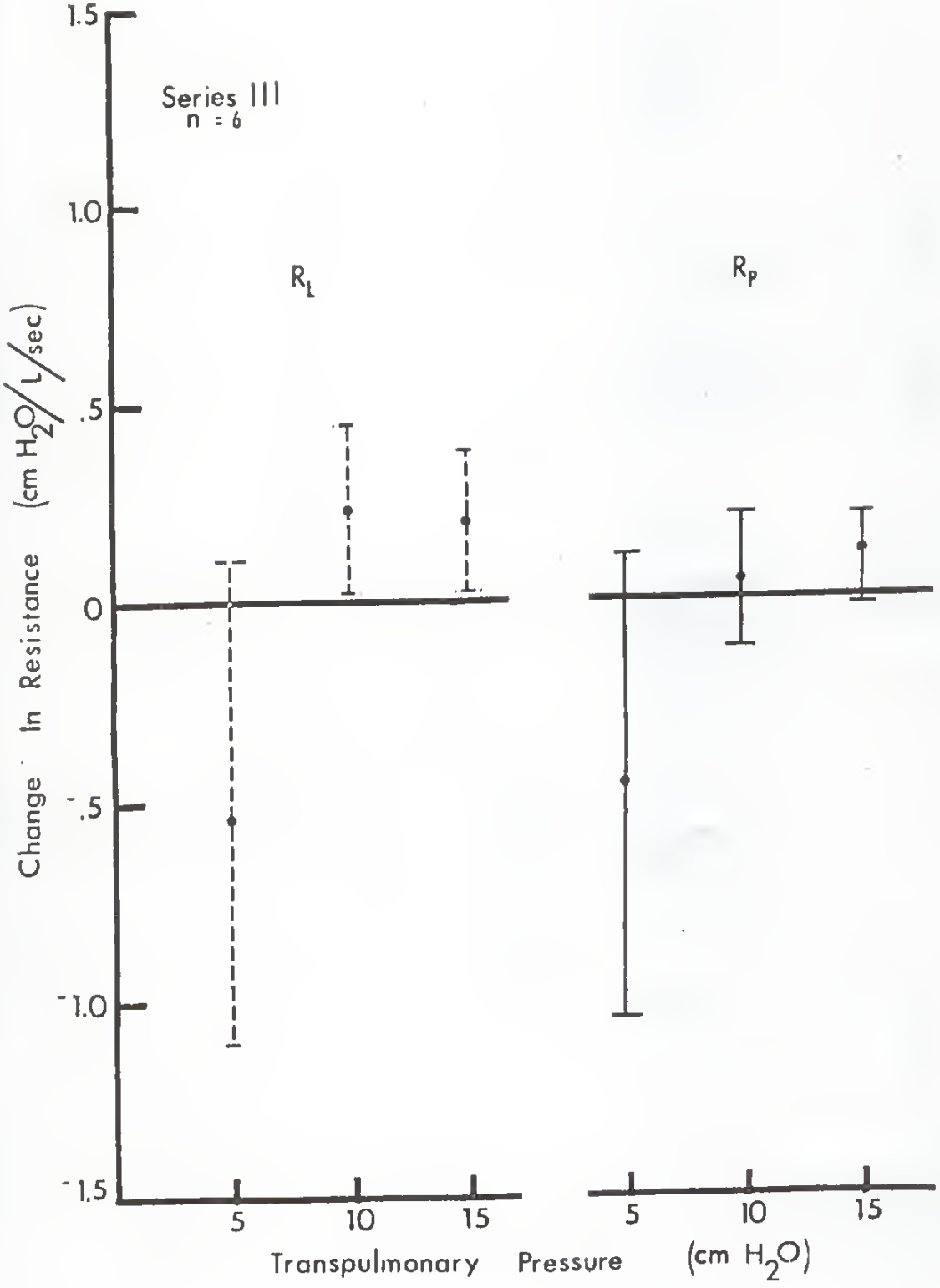

Series III
n = 6
R_L
R_P
1.5
1.0
.5
0
-.5
-1.0
-1.5
Change In Resistance (cm H_2O/L/sec)
5
10
15
5
10
15
Transpulmonary Pressure (cm H_2O)

Table 6. Individual data for 6 dogs of series III. All values are in cm.H_2O/liter/second. C = closed chest, C+β = closed chest with beta adrenergic receptor blockade; O+β = opened chest with beta adrenergic blockade.

P_{tp}	5 cm H_2O						10 cm H_2O						15 cm H_2O					
	R_L			R_P			R_L			R_P			R_L			R_P		
Dog	C	C+β	O+β	C	C+β	O+β	C	C+β	O+β	C	C+β	O+β	C	C+β	O+β	C	C+β	O+β
14	5.22	9.24	6.45	1.89	2.82		2.15	1.77	1.28	1.05	0.96		1.86	1.91	1.24	1.28	1.47	0.79
15	1.19	1.02	0.90	0.42	0.46	0.33	0.95	0.96	0.91	0.42	0.45	0.35	0.97	0.97	1.28	0.49	0.62	0.59
16	2.11	2.38	2.61	1.42	1.60	1.77	1.38	1.70	0.98	0.88	1.06	0.71	1.62	1.59	1.25	1.17	1.15	0.94
17	1.72	2.44	5.13	1.12	1.43	3.85	1.30	1.59	2.00	0.80	0.85	1.39	1.19	1.14	1.54	0.75	0.69	1.05
18	3.01	3.02	2.53	2.08	1.83	1.37	1.54	1.89	1.14	1.01	1.26	0.59	1.70	1.36	0.97	0.89	0.79	0.63
19	2.46	1.74	1.34	1.11	0.86	0.67	1.34	1.49	0.88	0.63	0.68	0.43	1.15	1.26	0.90	0.57	0.66	0.48
$\bar{x}$	2.62	3.30	3.16	1.34	1.50	1.59	1.44	1.57	1.20	0.80	0.88	0.69	1.41	1.37	1.21	0.86	0.89	0.75
s.e.	0.57	1.21	1.29	0.24	0.33	0.61	0.15	0.13	0.17	0.09	0.11	0.18	0.14	0.13	0.08	0.12	0.13	0.08

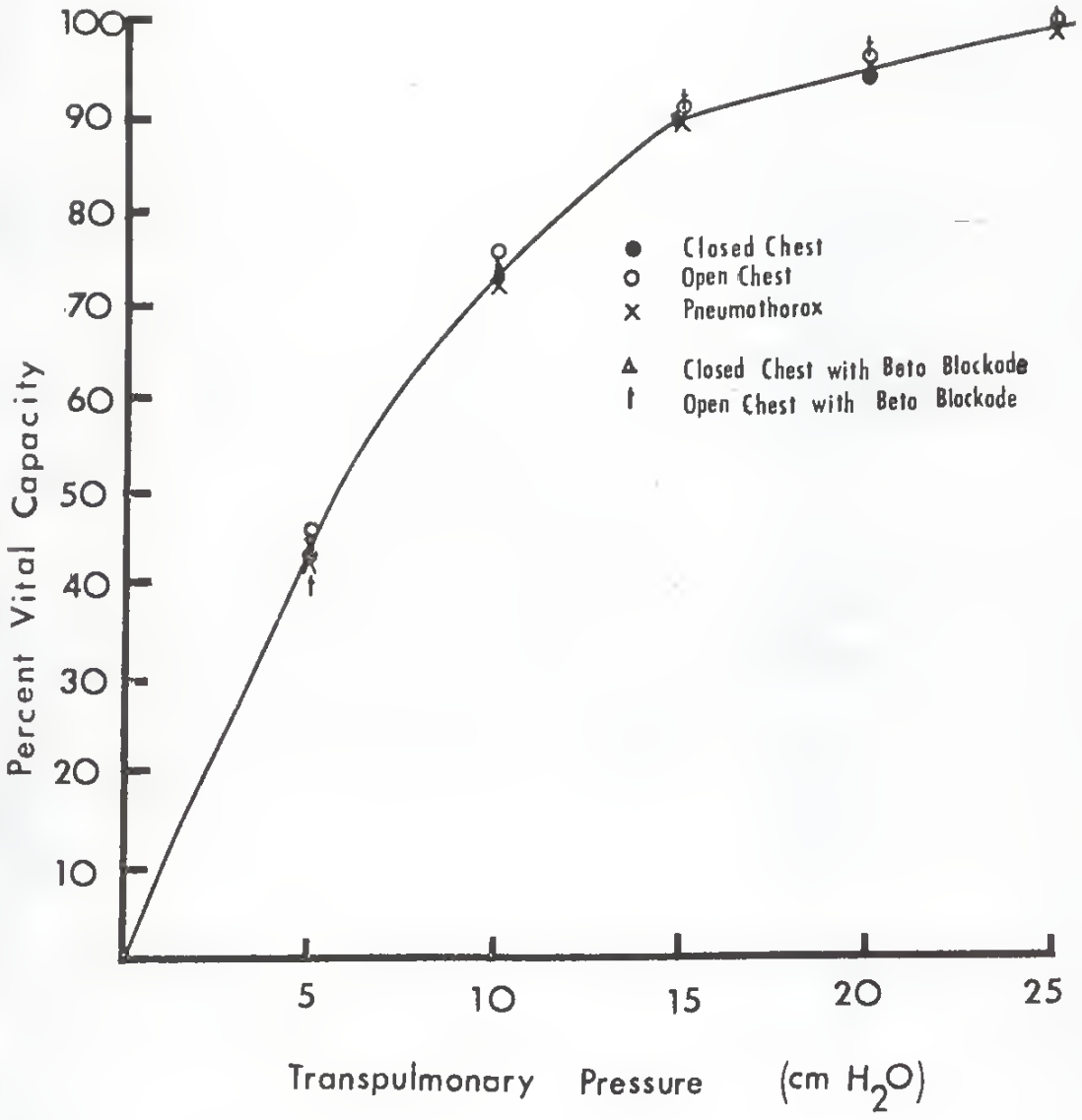
Figure 11 is a plot of the differences between the closed chest and the opened chest with beta adrenergic blockade for R_L and R_P as a function of P_{tp}. None of these values are significantly different from zero; however at a P_{tp} of 5 cm. H_2O there is a trend for the resistance in the opened chest with beta adrenergic blockade condition to be greater than the closed chest without beta adrenergic blockade.

Table 4 contains the individual data for the 6 dogs of Series III. Also included are the means and standard error of the means for each condition and each transpulmonary pressure.

Pressure Volume Curves

Figure 12 is a plot of lung volume as a percent vital capacity as a function of transpulmonary (P_{tp}) in the closed chest, closed chest with beta blockade, opened chest, opened chest with beta blockade conditions and in the case of a pneumothorax. Vital capacity was defined as the change in lung volume during a passive deflation from a P_{tp} of 25 cm. H_2O to 0 cm. H_2O with the chest opened. Each point represents the mean for each group. There were no significant changes in lung volume at any transpulmonary presure between the various conditions.

Figure 12. The volume of the lung as a percent of the vital capacity in the opened chest is plotted as a function of transpulmonary pressure.


100
90
80
70
60
50
40
30
20
10
Percent Vital Capacity
5
10
15
20
25
Transpulmonary Pressure (cm H_2O)
Closed Chest
Open Chest
Pneumothorax
Closed Chest with Beta Blockade
Open Chest with Beta Blockade

Transpulmonary pressure of 5, 10 and 15 cm. H_2O corresponds to 45.3, 74.4 and 97.5 percent of vital capacity, respectively.

Location of the Catheter

Table 5 contains the anatomical data obtained when the lungs were dissected after being dried at a transpulmonary pressure of 20 cm. H_2O for 3 days. Given are the diameter, distance from the carina and generation (trachea = 0) of the airway in which the catheter was wedged. The diameter ranged from 2.7 cm. to 4.0 cm. with a mean of 3.0 cm.

Blood Gases

Table 6 contains the means and standard deviations for the pH, P_{CO_2} and P_{O_2} of the 19 dogs. The control values were obtained with the dogs spontaneously breathing through a cuffed tracheostomy tube prior to placement of the catheter. All other values represent the periods indicated in the table. There were no significant alterations throughout the course of the experiments in the blood gas status of the dogs.

Table 7. Diameter, generation and distance from the carina of the airway containing the retrograde catheter for each experiment.

Dog	Diameter (mm.)	Generation	Distance from the carina (cm.)
1	4.0	5	7.0
2	2.7	6	8.6
3	3.2	7	8.9
4	3.0	7	9.0
5	2.7	10	10.0
6	2.9	9	8.7
7	3.1	7	7.7
8	3.0	9	8.9
9	3.1	9	8.8
10	2.8	8	9.0
11	2.8	5	9.0
12	3.1	6	6.0
13	3.6	5	7.0
14	3.3	7	8.3
15	2.7	10	9.3
16	3.0	8	9.0
17	2.9	8	7.6
18	3.2	7	8.0
19	2.9	9	10.0

Table 8. Mean and standard deviation for pH, P_{CO_2} and P_{O_2} at the indicated time in the experimental procedure.

	P_{O_2}	P_{CO_2}	pH
Control	79.1 ± 5.6	39.2 ± 3.8	7.34 ± .04
Catheter in Place	78.9 ± 6.7	39.4 ± 2.4	7.34 ± .02
Closed Chest	80.8 ± 6.4	38.7 ± 3.0	7.34 ± .03
Closed Chest and β blockade	77.6 ± 8.2	41.8 ± 3.6	7.33 ± .03
Pneumothorax	79.6 ± 5.6	38.6 ± 2.9	7.35 ± .01
Open Chest	78.5 ± 6.7	38.8 ± 2.9	7.36 ± .02
Open Chest and β blockade	79.0 ± 6.4	42.0 ± 3.2	7.32 ± .03

DISCUSSION

Experimental Design

In order to minimize animal variability, measurements of resistance were made on a paired basis, that is, each dog served as its own control. The coefficient of variation (standard deviation/mean x 100) for R_L for all dogs at a transpulmonary pressure of 5 cm H_2O was 41%. This is a smaller value than that found by other authors (36). The variability was, in part, due to the fact that the dogs were of a different size, age and breeding. Since R_L is dependent on lung volume any error in the volume at which the measurements were made would increase the variability in R_L. The coefficient of variation for R_P at a transpulmonary pressure of 5 cm. H_2O was 59%, a value also smaller than that of previous investigators (36). The variability in R_P can be explained on the same basis as the R_L variation. In addition, R_P is dependent on the location of the retrograde catheter, which may account for some of the variability between dogs.

Measurements of R_P and R_L within the same dog at a

given condition were reproducible. For example, the average coefficients of variation for R_L and R_p in the closed chest condition at a transpulmonary pressure of 5 cm. H_2O for the 13 dogs of series I were 18% and 20%, respectively. This variability may be related to an error in the lung volume at which repeated measurements were made since both R_p and R_L are lung volume dependent. The remaining variability is either due to measurement error and/or random changes in resistances between measurements.

Since the experiment was designed to test the effect of various conditions on the contribution of peripheral resistance to lower pulmonary resistance it was necessary to maintain as many factors as possible, other than those to be tested, constant between conditions. The level of anesthesia and muscle paralysis were maintained constant throughout the experiment and should not have influenced the resistance between conditions. Since the arterial pH, P_{CO_2} and P_{O_2} were unchanged in the various conditions they should not be responsible for changes of resistance between conditions. The lungs were always inflated to a transpulmonary pressure of 25 cm. H_2O prior to oscillation which means there was a common lung volume history in all the conditions. The lack of change in the quasi-static pressure volume curves indicates that there were no changes in

overall elastic properties of the lungs between conditions and that the lung volume for the paired transpulmonary pressures was the same. This means that the resistances for the different conditions were measured at the same lung volume. This does not necessarily imply that the geometry of the airways was the same in all conditions. It would be possible for a change in the shape of the lung to have occurred or for the distribution of the volume between the various sized airways and the alveoli to have been altered between conditions In the opened chest condition the influence of the chest wall on the shape of the lung is lost as is the influence of gradients of pleural pressure. Either of these changes could result in a change of distribution of volume, which would not be detected by a static pressure volume curve.

Methods

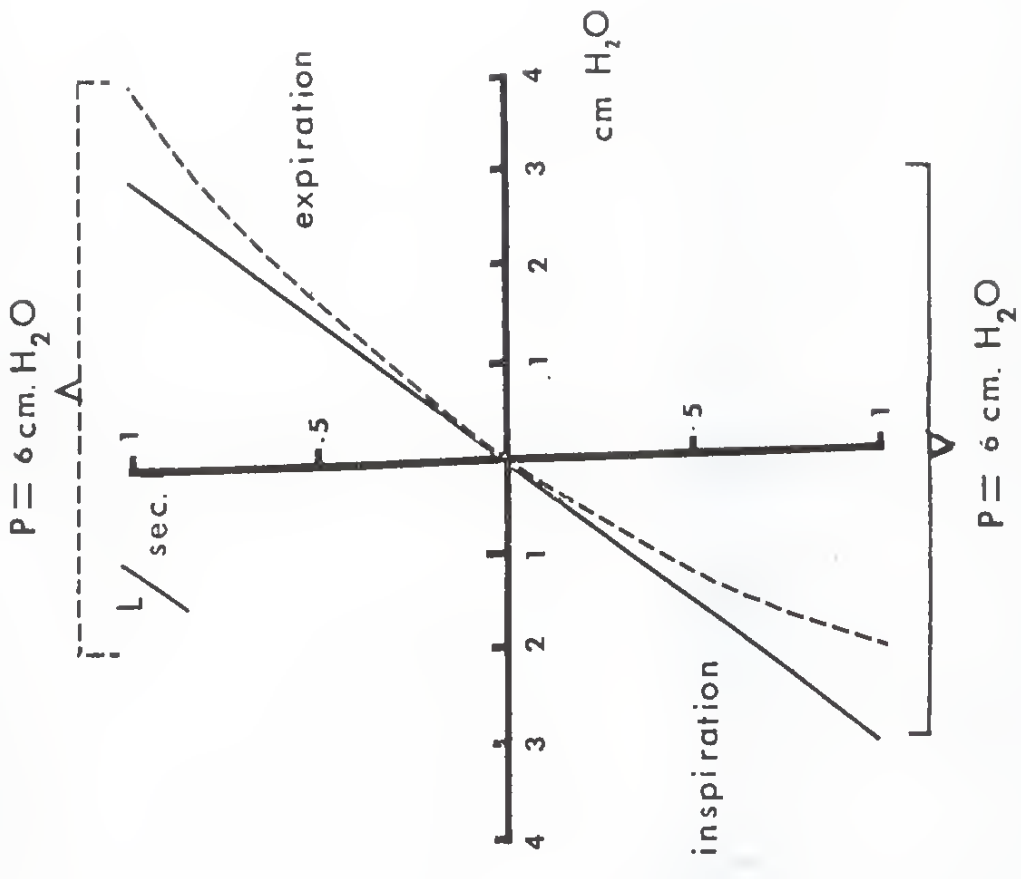
As previously described, the measurement of R_p and R_L in all conditions was done by the same technique. If errors were made in the determinations of resistance there is no reason to suspect that such errors would not be common to all conditions. That is, a change in resistance between conditions should not be explainable by any systematic error in measurement.

The lack of an asymmetrical pressure flow loop was surprising since, as was previously shown, there should have been errors in the measured pressure drop due to the Bernoulli effect. Its absence suggests an inadequacy of the measurements or that the effect is masked by the technique of closing the loop during oscillation by electrically substracting a proportion of volume.

Figure 13 is designed to describe the effect, in theory, of the Bernoulli principle. It is a plot of pressure vs flow with an assumed resistance of 3 cm. H_2O/liter/second. The solid line is the ideal plot. The dashed line shows the shape of the pressure flow plot for the conditions described above with the inclusion of the Bernoulli effect when the pressure drop is measured between the alveolus and a tracheal tube 1 cm. in diameter.

Since the pressure drop was measured as the peak to peak amplitude from a recording of pressure against time the calculated resistance would be independent of any Bernoulli effect. This can be seen in Figure 13 by comparing the peak to peak pressures for the ideal and the asymmetrical pressure flow plots. Moreover, since the linear velocity at the point of the bronchial pressure measurement is less than at the trachea any influence of the Bernoulli effect on R_p would be smaller than that for

Figure 13. Plot of a theoretical pressure flow curve with (dashed line) and without (solid line) the predicted influence of the Bernoulli effect.


P = 6 cm. H_2O
L / sec.
1
.5
expiration
cm H_2O
4
3
2
1
.1
.5
1
inspiration
P = 6 cm. H_2O

R_L. Again there is no reason to suspect that the Bernoulli effect would be different in any of the different conditions and therefore it can not explain changes in resistance between conditions.

It is clear that the flow resistance measured during the oscillatory technique includes tissue viscous resistance as well as resistance to air flow. Various authors (6,9,16,17) have measured tissue resistance and arrived at values as low as 4% and as high as 40% of the pulmonary resistance. Bachofen (2) has shown that tissue resistance increased with increased tidal volume when flow rate and functional residual capacity were held constant. It was also observed that doubling flow rate without changing tidal volume or end expiratory volume did not appreciably increase the non-elastic work performed on the lung, so tissue resistance had to have decreased (1). These results suggest that tissue resistance does not behave as a flow resistive element but as a non-ideal elastic element exhibiting pressure volume hysteresis.

Marshall and Dubois (16) have shown that the measured tissue resistance is reduced by panting compared to that observed at normal breathing frequencies. Wood (34) has calculated the tissue resistance for a healthy human assuming a flow of 1 liter/second, a compliance of 200 ml./cm.H_2O and resistance of 2 cm. H_2O/liter/second for several

frequencies. At a breathing rate of 10 breaths/minute with a tidal volume of 1000 ml. he predicted that 30% of the resistive work done on the lung could be accounted for by tissue resistance. At a frequency of 100 breaths/minute and a tidal volume of 100 ml. tissue resistance accounts for only 3% of the resistive work done on the lung. When the lung is oscillated at a frequency of 4 cycles per second with a volume of 40 ml. the contribution of tissue resistance to the resistive work becomes negligible. For these reasons the resistance measured during the present experiments is considered to reflect predominantly airway resistance and not tissue resistance.

Comparison of R_p Measured in Vivo With Predicted Values Based on Anatomic Data

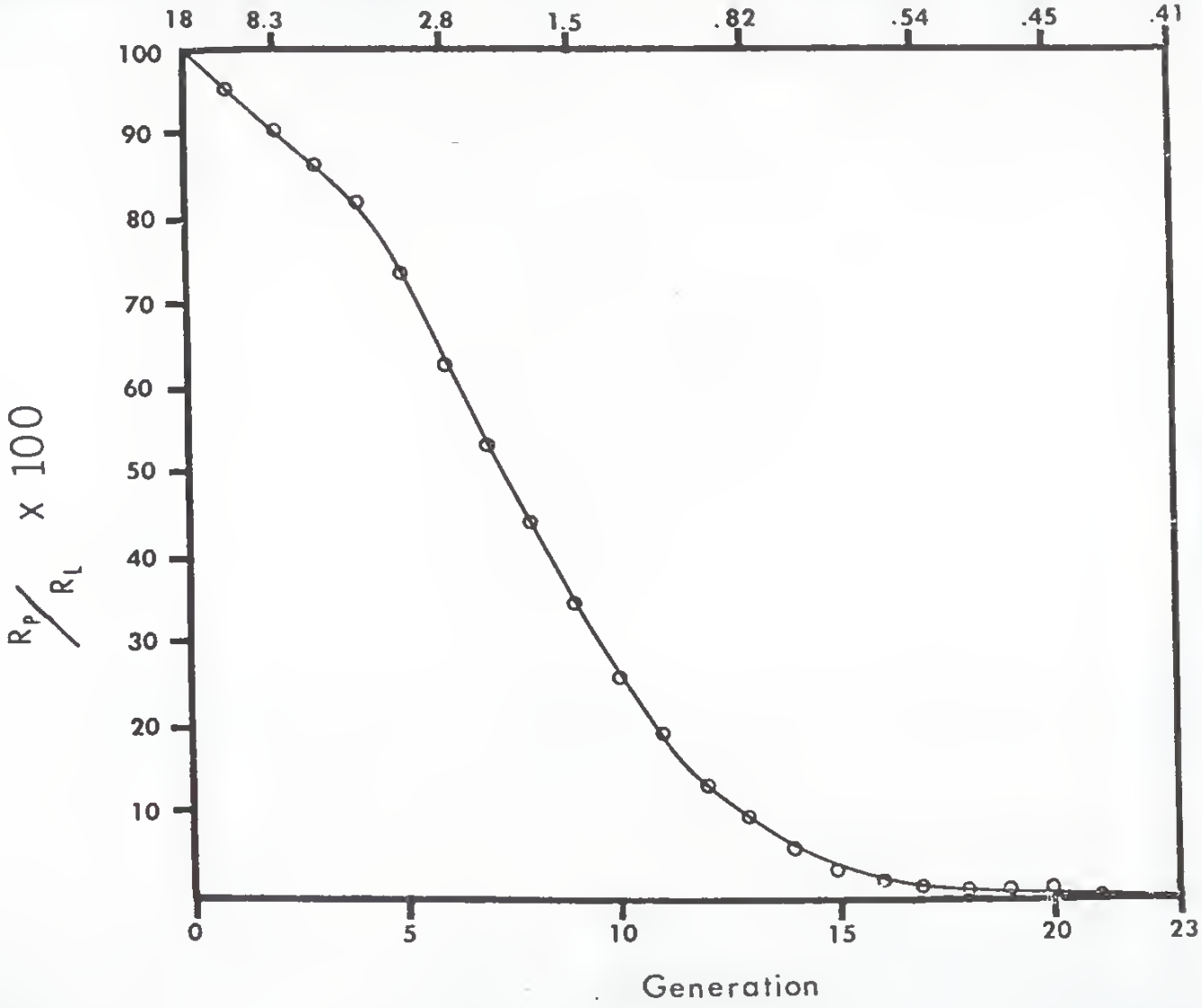
Ross (26) has conducted an extensive study of the structure of the bronchial tree in the dog. Using a plastic cast he was able to measure airways down to 0.5 mm. in diameter and up to 8 generations in number. He found that bronchial pathway lengths from the carina to terminal bronchioles, which he defined as airways 1 mm. in diameter, were quite variable and ranged from 2-14 cm. In the human lung the distribution of 2 mm. airways is from 3 to 30 cm. from the carina, a distribution similar to the dog for 1 mm.

airways. Horsefield and Cumming (8) found that the number of terminal bronchioles arising from a bronchus of a given cross-sectional area decreased the farther it arose from the carina. Ross (26) reported a similar finding in the dog lung. Irregular branching, the distribution of terminal bronchioles and the factors determining the number of terminal bronchioles arising from a bronchus of given cross-sectional area are similar to both the human and dog lung, suggesting that the dog lung may be an appropriate model for studying airway resistance.

Green (7) has used Weibel's (31) anatomical data for the human lung to compute the resistance in each generation assuming laminar flow. Figure 14 is a plot of the R_P to R_L ratio using these predicted resistances. This is an original plot and does not appear in Green's paper. It can be seen that airways 2.8 mm. and less in diameter contribute more than 50% to lower pulmonary resistance. This agrees well with the experimental results obtained in dog with the chest intact near functional residual capacity.

Ross (26) developed an equation to describe the pressure gradient across a unit length of any bronchus in terms of the relative pressure gradient across the same length of trachea for any flow rate. The differences in flow rate in the trachea and bronchus are taken into account in this

Figure 14. The resistance of the bronchi of a given generation and those peripheral to that generation is plotted as a percent of the total bronchial resistance. The abscissa is a linear scale of generation number. The corresponding diameters are also shown.


18
8.3
2.8
1.5
.82
.54
.45
.41
100
90
80
70
60
50
40
30
20
10
0
5
10
15
20
23
R_p/R_L x 100
Generation

relationship:

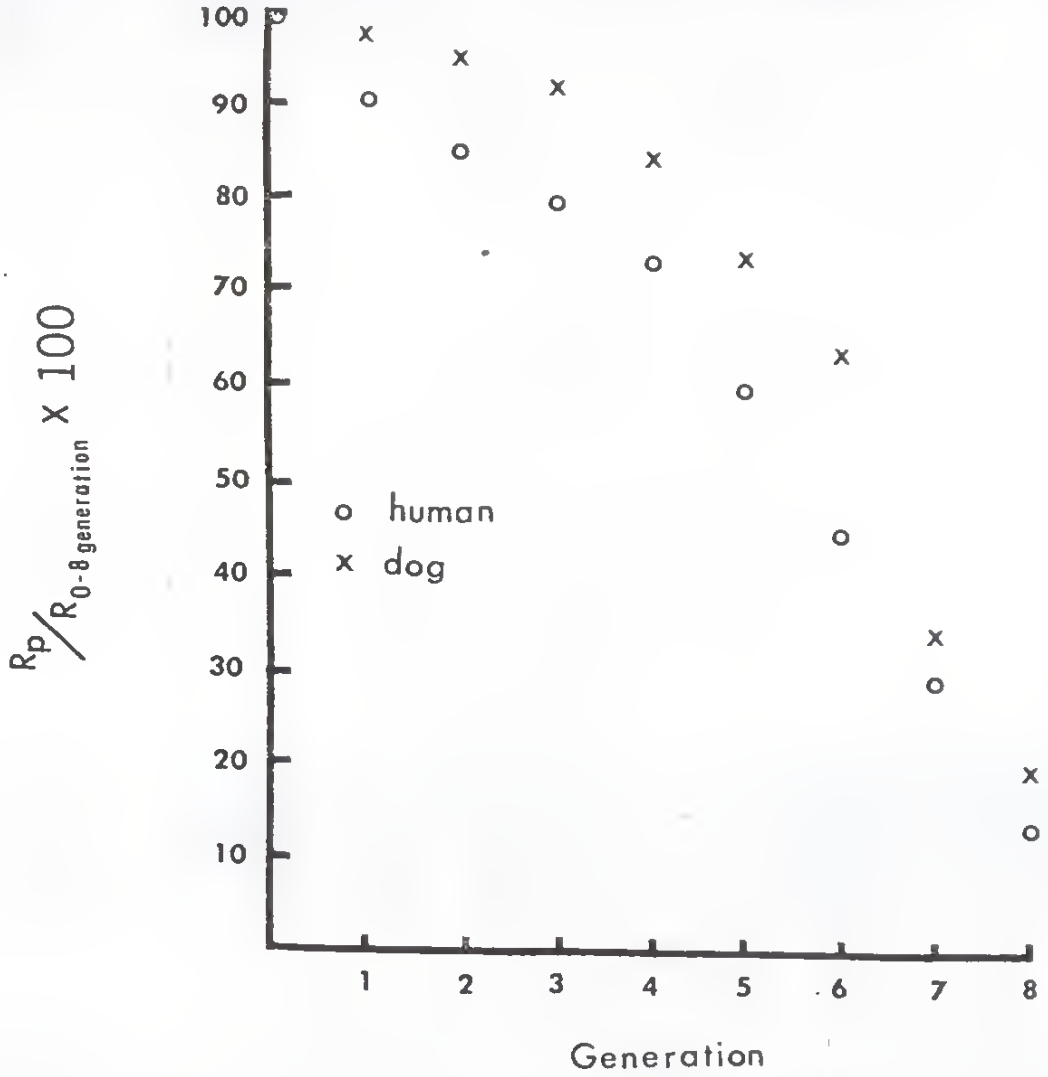
$$\% \left(\Delta P/L\right)_{trachea} = \frac{3300}{A^{.75}(D+2)^{.5}}$$

A = cross-sectional area

D = distance from carina

Using this equation and the anatomical data of Ross (30) the pressure drop per generation for 3 randomly selected bronchial pathways was calculated. The mean for these three pathways results is plotted as a R_P/R_L ratio where R_L is the resistance from trachea to the eighth generation in Figure 15. Since data for the dog were available for only the first eight generations the relationship for the human lung is also plotted for only the first eight generations. In the dog 40% of the resistance in the first eight generations is predicted to be beyond the sixth generation. In the human lung 30% of the resistance of the first eight generations is predicted to be beyond the sixth generation. It is clear that there are 15 generations beyond this level, which are not included in this theoretical treatment. The added resistance of these generations would result in an increased lower pulmonary resistance and can only increase the percentage of R_L contributed by the peripheral airways.

Figure 15. The resistance of a given generation and those peripheral to it is plotted as a percent of the total resistance of the first eight generations. The open circles (O) are based on Green's predictions for the human (7) and the (X) are based on Ross' data (26) for the dog.


$R_p/R_{0\text{-}8\,generation} \times 100$
100
90
80
70
60
50
40
30
20
10
o human
x dog
1
2
3
4
5
6
7
8
Generation

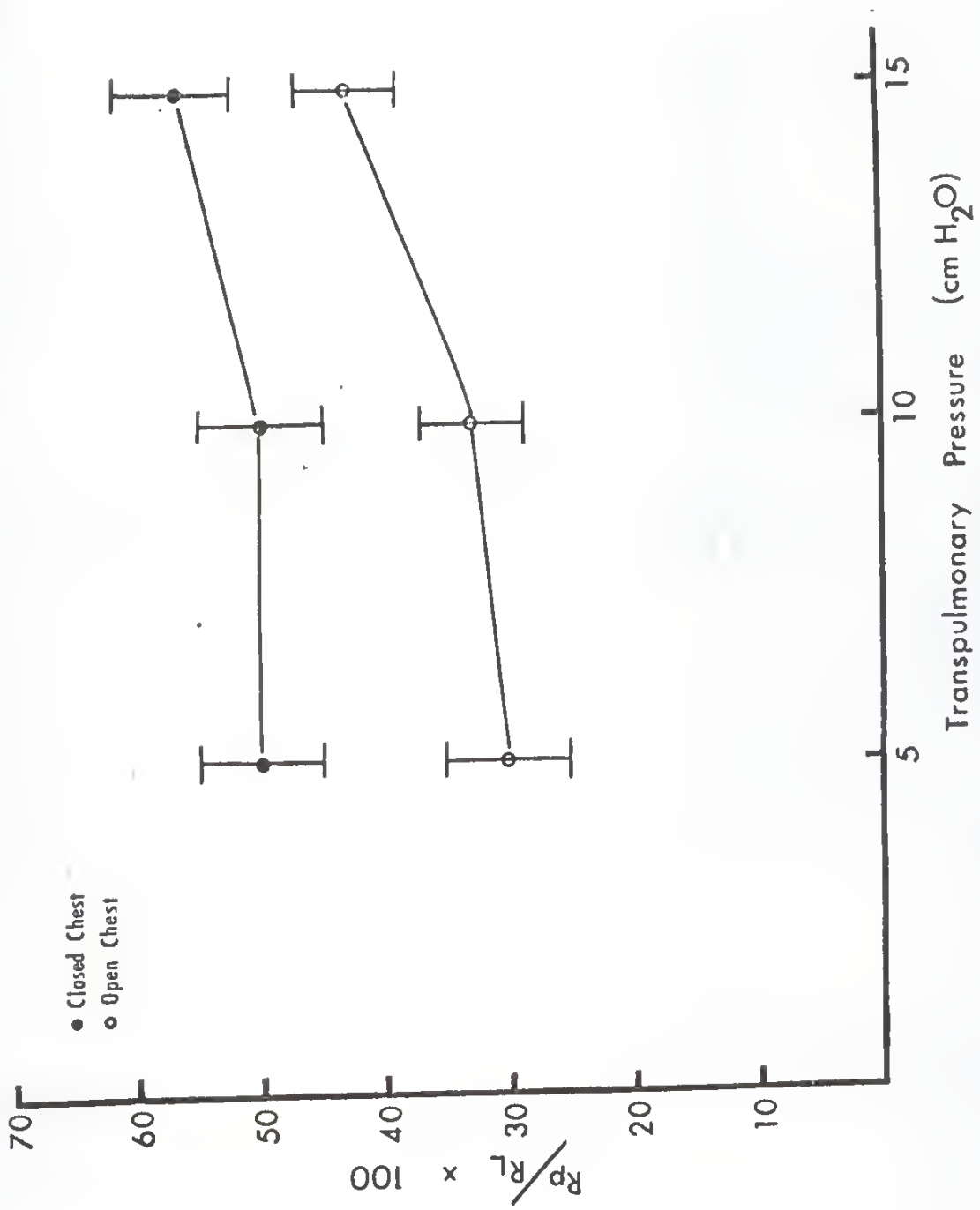
The Dependence of R_p and R_L on Lung Volume

The dependence of R_L on lung volume reported by previous investigators (33) was also observed in the present experiments. Woolcock et al.(35) have shown that the decrease of central airway resistance with increasing volume is reduced by vagotomy. Widdicombe and Nadel (33) found that vagal efferent impulses increase as lung volume decreases. This evidence suggests that there is a reflex mechanism by which bronchomotor tone increases as lung volume decreases. Since only small changes of R_p with lung volume were observed the present experiments confirm that it is mainly airways larger than 3 mm. in diameter that are responsible for the lung volume dependence of R_L.

The peripheral resistance showed an upward trend at 15 cm. H_2O pressure. Olsen et al. (22) have shown that the compliance of the airway is reduced at high transpulmonary pressures, which means the change in cross-sectional area of the airway at high P_{tp}'s is small. If the airway continues to lengthen at high P_{tp}'s as lung volume increases, while the area does not change, one would predict an increased resistance based on the Poiseuille relationship.

Since R_L was lower at the high lung volumes and R_p was not reduced at these volumes, the R_p to R_L ratio increases with increasing lung volume. The ratio is shown in Figure 16

Figure 16. The mean peripheral resistance as a percent of lower pulmonary resistance with the chest closed (●) and opened (○) is plotted as a function of transpulmonary for the 13 dogs of series I. One standard error of the mean is shown above and below the mean.


• Closed Chest
o Open Chest
70
60
50
40
30
20
10
R_P/R_L x 100
5
10
15
Transpulmonary Pressure (cm H_2O)

for the 13 dogs of series I. This result agrees with that of Woolcock et al. (35) and is in direct contradiction with the findings of Macklem and Mead (13).

The Changes in Resistance Induced by Opening the Chest

In series I a reduction of peripheral resistance (R_p) at all lung volumes was observed when the chest was opened. The reduction of R_p was the smallest at the highest lung volume. There may be a mechanical explanation for this observation. Near total lung capacity even with the chest widely split, the shape of the lung is still somewhat influenced by the chest wall. If the peripheral resistance is reduced in the opened chest because of geometrical changes related to the removal of the chest wall then a reduction in the difference between R_p in closed and opened chest would be expected at high lung volumes.

Induction of a pneumothorax without the splitting of the sternum and the spreading of the chest does not result in a reduction of R_p. This indicates that the removal of the negative pleural pressure and equalization of the pleural pressure in the thorax is not the cause of the difference in R_p between the closed and opened chest. Since the chest wall expands when a pneumothorax is produced, the chest should have less influence on the shape of the lung at low lung

volumes. If the reduction of R_p in the opened chest condition is related to the lack of influence of the chest wall on lung shape a reduction of R_p would have been expected at the low transpulmonary pressures but was not seen.

Woolcock et al. (35) have demonstrated in the opened chest dog that vagal influences exist throughout the bronchial tree in the dog. They observed a wide variation in the response of central and peripheral airways in different dogs to vagal stimulation. They hypothesized that the distribution of vagal fibers along the tracheobronchial tree varies from dog to dog and suggested this as an explanation for the variability in response among dogs to vagal stimulation. In another study, also in the opened chest dog, Woolcock et al. (36) demonstrated increased responsiveness to vagal stimulation in both the central and peripheral airways when beta adrenergic receptors were blocked. Propranolol, itself, doubled R_p and reduced R_c resulting in an unchanged R_L.

In the present study beta adrenergic receptor blockade did not result in a significant change of R_p or R_L in the closed chest dog. However, it did prevent the 50% reduction of R_p which had been observed in the non beta adrenergic blocked dogs when the chest was opened. This can be thought of as having doubled the opened chest R_p, an effect of

propranolol equal to the magnitude of that observed by Woolcock et al. (36).

The lack of an effect of beta adrenergic receptor blockade on R_L or R_p in the closed chest dog agrees with the findings of Tattersfield et al. (30) in the intact human. They found in six normal subjects that propranolol did not alter airway conductance, lung volume, maximal and partial expiratory flow volume curves, expiratory static pressure volume curves or dynamic lung compliance. Beta adrenergic receptor stimulation with Salbutamol increased airway conductance in 3 of 4 subjects indicating the presence of resting bronchomotor tone.

The lack of a response to propranolol in the closed chest dog and the presence of a response in the opened chest dog suggest an increase of beta adrenergic receptor stimulation occurs in the peripheral airway when the chest is opened. This would result in a reduced resistance and provides an explanation for the observed effect on R_p of opening the chest. However, it does not explain the increase of R_c which must have occurred to maintain R_L constant when the chest is opened. It is possible that there is also an increased parasympathetic tonus when the chest is opened. In the central airways where these fibers are predominant an increased resistance would be observed,

while in the periphery where the sympathetic fibers predominate a reduced resistance would be observed.

Widdicombe (32) has suggested that ganglia in the region of the bronchi could mediate local reflexes in the bronchial tree. This could be the mechanism of the increase of R_C when R_P decreases. Propranolol would not block the increase of R_C when the chest is opened if it is due to an increase in parasympathetic tone. In the present experiments, propranolol blocked the reduction of R_P and no significant increase of R_L was observed. If R_C increased and R_P was unchanged R_L should have increased. This suggests that an increase in R_C may occur as a reflex response to a reduction in R_P.

This reflex between large and small airways could be studied by infusing a smooth muscle relaxant into the pulmonary circulation which should dilate peripheral airways since they receive their blood flow from pulmonary capillaries and cause a reflex increase in R_C. Prostaglandin E_1 would be an appropriate drug to test this hypothesis since it would not have any systemic effects because of its inactivation when it passes through the lung. If a response in the central airway was observed the effect of vagotomy on the response could be tested to determine wheter the reflex was local or centrally mediated.

It is still unclear as to how sympathetic stimulation could have a predominant effect in the periphery. It could be due to an increased number of beta adrenergic receptors in peripheral airway smooth muscle or increased number of nerve endings. The possibility also exists that sympathetic fibers end predominantly in the precapillary vasculature. Lockett (10) has shown that sympathetic stimulation causes an increase in catecholamine like substances in the pulmonary venous effluent. This substance would selectively influence peripheral airways since they are perfused by the pulmonary circulation.

In future experiments, it would be beneficial to record heart rate as a method of evaluating changes of sympathetic and parasympathetic tone in the whole animal. If the hypothesis is correct that there is an increase in both systems then no change in rate should be observed. If parasympathetic predominates then heart rate should decrease while the opposite is true if sympathetic predominates. It may also be of interest to test the effect of vagotomy on the resistance response to opening the chest. This would provide information concerning the increase of R_C when R_P is reduced.

In summary it has been shown on a predicted basis and by actual measurement that airways less than 3.0 mm. in

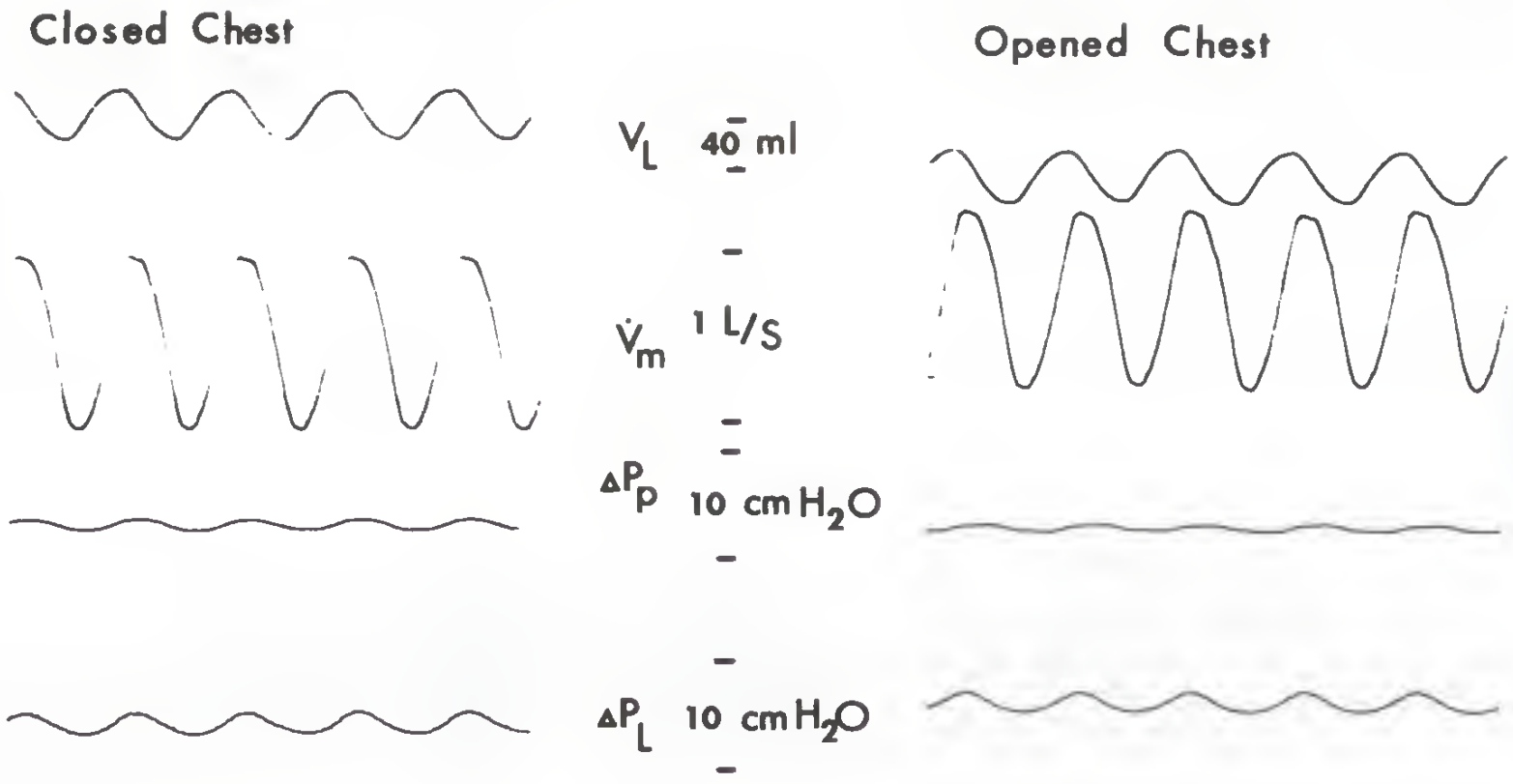
diameter contribute up to 50% of lower pulmonary resistance or approximately 25% of the total airway resistance. Measurements of R_p made in the opened chest dog are significantly reduced because of an increased beta adrenergic receptor stimulation. It is suggested that any measurements of peripheral resistance made in the experimental animal should be done with the chest intact if meaningful results are expected.

APPENDIX

A typical recording from one experiment is shown in Figure A.1. The peripheral pressure drop (ΔP_p) and lower pulmonary pressure drop (ΔP_L) are plotted as a function of time during oscillations at 4 cycles per second.

As described in the methods these pressure drops are due to resistance and can be related to flow at the airway opening to obtain resistance. The peak to peak pressure drop was related to the peak to peak flow to obtain resistance for the peripheral airway and the lower pulmonary airways.

Figure A.1. Recording of data from a typical experiment with the chest closed and following a sternal splitting procedure. Volume (V_L), flow ($\dot{V}_M$), peripheral pressure drop (ΔP_p) and lower pulmonary pressure drop (ΔP_L) are plotted as a function of time.


Closed Chest
Opened Chest
V_L 40 ml
$\dot{V}_m$ 1 L/S
ΔP_p 10 cm H_2O
ΔP_L 10 cm H_2O

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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